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DRUG ERUPTIONS

II. DERMATITIS ECZEMATOSA DUE TO DRUGS

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In a previous article on drug eruptions,[1] we discussed mainly fixed phenolphthalein eruptions and came to the conclusion that in these, except for the ingestion test to be mentioned, neither skin tests nor any other forms of testing have been evolved which are of value in diagnosis and in proving existing hypersensitiveness to the drug. We believe this to be true in practically all drug eruptions of non-eczematous and nonurticarial type. (The passive transfer experiments of Biberstein[2] and others are still much too complicated, much too uncertain and irregular, and too doubtful in their significance to be of aid in individual cases.) We are, therefore, in the case of fixed eruptions, reduced to the unsatisfactory, sometimes dangerous or impossible expedient of waiting until an eruption subsides and then administering the suspected drug (ingestion test).

In the eczematous drug eruptions,[3] the situation in regard to testing is much more favorable, for the epidermis is in all probability the seat of the sensitiveness. The reaction is a dermatitis eczematosa, and contact or patch tests are of great aid. It was, in fact, an observation in a case of mercurial dermatitis of erythematous and eczematous type which led J. Jadassohn[4] first to employ this form of testing.

The response to the patch test does not seem to differ in cases which are due to contact from without (topical applications and industrial factors) and in cases due to contact from within (e. g., hematogenic distribution following internal medication). Provided the cutaneous response to the drug is *eczematous* and *vesiculating*, the

1. Wise, Fred, and Sulzberger, M. B.: Drug Eruptions: I. Fixed Phenolphthalein Eruptions, Arch. Dermat. & Syph. **27**:549 (April) 1933.

2. Biberstein, Hans: Beiträge zur passiven Uebertragung der Ueberempfindlichkeit gegen chemisch bekannte Stoffe, Jena, Gustav Fischer, 1926.

3. It seems likely that phenolphthalein can cause eczematous dermatitis as well as fixed eruptions. However, the former type of reaction seems to be extremely rare. We have seen but one case with a strongly positive eczematous reaction to phenolphthalein patch tests.

4. Jadassohn, J.: Zur Kenntnis der medicamentösen Dermatosen, Vienna, Wilhelm Braumüller, 1896.

pathologic processes are apparently identical and, in most cases, can be demonstrated by external application. Bloch [5] has repeatedly called attention to this fact.

The designation "dermatitis eczematosa due to drugs" may, at first, appear complicated, but it is the only term we can think of which does not imply a certain manner of contact and thus includes all eczematous drug eruptions, whether the drug reaches the skin from within or from without.

While the manner of distribution to the skin is of clinical importance, from the immunologic point of view which we are discussing here, the process seems essentially the same, no matter by which route the drug arrives. The case of E. L., described in more detail in our first article,[1] illustrates this point.

The patient first had a vesicular and weeping dermatitis of the scalp, face, hands and arms, due to contact with a hair lotion containing quinine. Over one year later, she suffered from erythrodermia involving the skin of the whole body and an acute weeping dermatitis on the previously affected areas. This time the eruption was due not to external contact but to the hematogenic distribution of quinine contained in a "bromoquinine laxative" tablet which the patient had taken by mouth.

In this case the first eruption was a dermatitis venenata due to external contact with quinine; the subsequent generalized eruption was a dermatitis medicamentosa due to the ingestion of quinine, and the persistent areas of the second eruption were a condition which must be called a dermatitis medicamentosa in some way influenced by a preceding dermatitis venenata. The appellation "drug eruption of eczematous type" or "dermatitis eczematosa due to quinine" describes all three manifestations and brings them under the one logical classification which their common etiology, common clinical and histologic appearance and common immunologic status seem to render desirable.

CASES OF BUTESIN PICRATE DERMATITIS

An excellent opportunity for further observation in drug eruptions of eczematous type was afforded by the following four cases of butesin picrate dermatitis.

CASE 1.—*History.*—Mrs. L. S., aged 26, burned the extensor surface of her forearm above the left wrist and the flexor surface of the forearm above the right wrist on Oct. 20, 1931. In both areas the epidermis was destroyed to a great extent. Immediately after burning herself, she applied to the wrist an ointment containing 1 per cent of butesin picrate; she continued to use this preparation for one week. At the end of that time, the skin had reassumed an almost normal appearance and the applications of ointment were stopped. On November 4

5. Bloch, Bruno: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:175 (Feb.) 1929.

(approximately two weeks after the first application of the ointment and one week after its use was stopped) itching and burning began on both the areas to which the ointment had been applied. These symptoms increased steadily, and on November 20 (more than four weeks after the first application) an eruption appeared on both forearms.

At the first examination (Nov. 20, 1931) we observed an erythematous and weeping dermatitis, with acute vesicle formation. This occupied the points of contact with the ointment and was associated with diffuse edema of both arms (their circumference was approximately double the normal) which extended to the shoulders. The nonerythematous swelling of the arms was said to have developed several days after the appearance of the acute erythematous dermatitis on the forearms and wrists. The skin of the upper extremities not involved in the acute dermatitis appeared almost normal, with the exception of the diffuse brawny edema and the implication of the follicles. The appearance of the follicles merits description. Each follicular opening was transformed into a vesicle or succulent papule the size of a small pinhead. These could be better felt than seen. There were severe itching and discomfort in the arms, the skin being extremely tender in the swollen areas. At the exact sites which had been occupied by the burns, areas irregular in shape and larger than a silver dollar, above the wrists, the skin was normal. These areas were not scarred or atrophied, but presented sharply defined islands of normal skin surrounded by the acute, vesicular, erythematous and weeping dermatitis (similar to the eruption in case 2, shown in the figure).

The course of the disease was surprisingly chronic. Ten days after the first examination, the patient began to complain of maddening pruritus over the entire body. There were no objective manifestations on the skin other than those described on the arms. The dermatitis and swelling gradually healed under wet dressings; the generalized itching persisted in its original intensity for four days and then gradually subsided. Furuncles began to appear on the previously affected areas and required treatment. It was only on Dec. 19, 1931, approximately two months after the use (and discontinuance) of the ointment, that the patient could be discharged as cured.

Patch Tests.—Patch tests were performed on unaffected areas of skin at different dates:

1. Butesin picrate ointment (1 per cent): The reaction was positive (3 plus). After twenty-four hours there was definitely palpable edema which seemed to penetrate deeply into the cutis. After seventy-two hours, each follicle was transformed into a small vesicle, and the test site presented an appearance identical with the clinical picture described on the arms. The reaction increased in intensity during six days after removal of the ointment; at no time was pronounced erythema present.

2. Butesin solution (1 per cent in alcohol): After twenty-four hours the reaction was strongly positive (4 plus). It was of the same type as in the first test, but much more marked, with slight erythema and very deep edema. Again the follicles were selectively affected.

3. Picric acid (saturated solution): After twenty-four hours there was no sign of a reaction, nor was there a reaction to picric acid (trinitrophenol) at any subsequent time of observation.

4. Ethyl aminobenzoate (1 per cent solution): After twenty-four hours the reaction was positive. It was of the same type as that in the first two tests, but milder than the response to butesin.

In addition, tests with the following preparations were negative: 1 per cent solution of benzoic acid and 1 per cent solution of salicylic acid.

Case 2.—*History.*—Mrs. C. L. P., aged 28, burned her left forearm with fat on March 12, 1931. The burn was superficial, but according to her description the epidermis was in great measure destroyed in an irregular area about 2½ by 2½ inches (7 by 7 cm.). One per cent butesin picrate ointment was applied to the burned area and the surrounding skin on the day on which the injury occurred, and the applications were continued for three days. Healing had then progressed so satisfactorily that the patient administered no further treatment and the skin became normal in appearance. On March 25 (thirteen days after the first and ten days after the last application of butesin picrate ointment) itching set in and a dermatitis began to appear at the site of application of the ointment. The dermatitis spread and increased in severity, and on April 5 Dr. J. J. Wiener of New York referred the patient to us for examination and treatment. Examination revealed a severe erythematous, weeping and blistering dermatitis on the left forearm and wrist and the dorsum of the hand. The arm and wrist were swollen. In the center of this acute inflammatory process, there was a relatively sharply demarcated nonaffected patch of irregular shape, about 4 square inches (25 sq. cm.) in area. Here the skin was practically normal in appearance, with only a very occasional, minute, scarcely visible vesicle and without redness (fig. 1). The affected area was said to correspond to the site of application of the butesin picrate ointment, and the island of normal skin to represent the site and shape of the original burn.

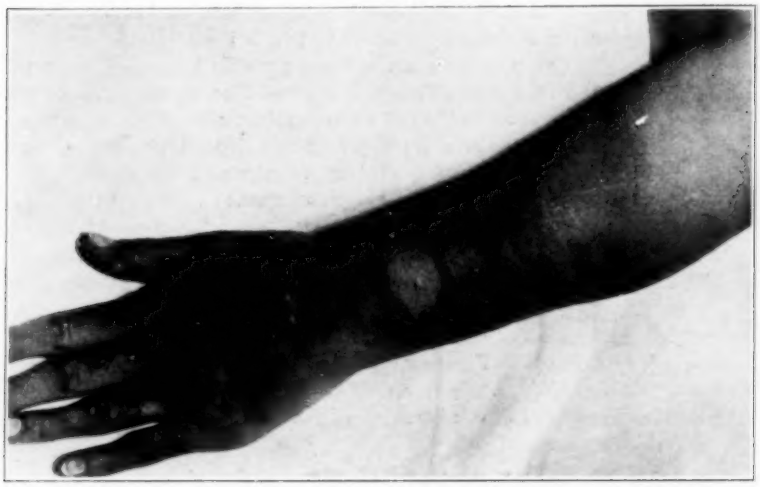

Fig. 1.—Dermatitis of the arm due to 1 per cent butesin picrate ointment (case 2). Photograph taken twenty-four days after the last application of the ointment, showing an island of practically unaffected skin occupying the previously burned area, from which the epidermis had desquamated, probably carrying with it the butesin picrate. Thus no residual excitant remained in the new cells at this area and no dermatitis ensued. This unaffected area of "new" epidermis proved to be hypersensitive when butesin picrate was subsequently applied.

It is worthy of note that many of the vesicles occupied the mouths of follicles, and that there were scattered follicular pustules throughout the entire affected area; this was particularly noticeable on the dorsa of the proximal phalanges, where only the follicular orifices were involved, the remaining skin being normal. (The picture here was not unlike that seen in some stages of pityriasis rubra pilaris.)

After application of wet dressings, healing was prompt and the course was without further complications.

Patch Tests.—Patch tests were made on the unaffected skin of the right forearm:

1. Butesin solution (1 per cent in alcohol): After twenty-four hours, the reaction was positive. However, the follicles were practically the only structures

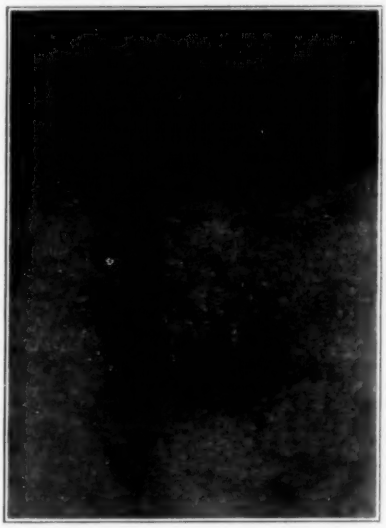

Fig. 2.—Photograph of the site of the butesin test in case 2, taken over one month after the application of a 1 per cent solution, illustrating both the persistence and the follicular nature of the reaction. (The reaction at the picric acid site, distal to the area shown, which had at first been severely inflamed and vesicular, and strongly erythematous but not infiltrated or follicular, had entirely disappeared more than two weeks prior to this date.)

visibly involved. There was marked edema at the site, and most of the follicles were transformed into prominent, hemispherical, pinkish papules larger than a pinhead.

2. Picric acid (saturated solution): After twenty-four hours, the reaction to picric acid (trinitrophenol) was strongly positive with intense erythema of the entire area. The surface was covered with very minute, closely agminated, non-follicular vessels.

3. Butesin picrate ointment (1 per cent). After twenty-four hours, the site presented a distinct combination of the reactions in the first two tests. There were several isolated large follicular papules scattered irregularly over an area

of diffuse erythema, together with numerous smaller, agminated, nonfollicular vesicles.

On April 12 (one month after the injury), we tested the "immune" site which had remained unaffected on account of the preceding burn. This site proved not to be "immune," but simply to have been unaffected, for it gave a typical eczematous reaction twenty-four hours after the application of a patch test with an ointment containing 1 per cent butesin picrate (fig. 2).

CASE 3.—*History.*—Mr. A. B., 38 years old, was first seen on Aug. 8, 1930. We were called in consultation by Dr. Harold T. Hyman of New York because of an increasingly severe and spreading dermatitis. When the patient was examined, there was a highly inflamed, reddened, greatly swollen, vesiculating and weeping dermatitis on the right elbow and the upper part of the right arm, midway to the shoulder. The entire affected area was covered with a yellow ointment. The anterior and lateral surfaces of the neck also presented a vesicular and weeping eruption. There were several areas covered with minute grouped vesicles, in the left axilla, on the left thigh and elsewhere on the body. Ten days previously, the patient had contracted a sunburn of the arms and shoulders and had applied (in addition to other remedies) a 1 per cent butesin picrate ointment. He had continued the use of the ointment as each application brought temporary relief from the burning and itching. In spite of this, the eruption grew worse and spread. The patient stated that two years previously he had used this ointment on a burn without ill effects. We ordered discontinuance of the butesin picrate and its removal with carbon tetrachloride and baths. We also commenced local therapy, including wet dressings and lotions. On the day of our first examination, we applied patch tests with the 1 per cent butesin picrate ointment and the other remedies that the patient had employed, all the tests being made on unaffected skin of the right forearm. The butesin picrate ointment caused such severe burning and itching that it had to be removed within six hours. The following day the site was reddened, swollen and vesiculating. All the other patch tests were negative.

In spite of therapy, the patient continued to grow worse. While the original dermatitis improved, one area after another became affected and presented a new outbreak of vesicles and dermatitis. There was also a very severe generalized and uncontrollable pruritus. The hands became affected, presenting deep-seated, sago-like vesicles identical in appearance with those seen in dermatophytids. The ears, the scalp, the scrotum and the intergluteal fold were next affected by the dermatitis. One week after the use of butesin picrate was discontinued (Aug. 15, 1930), deep-seated, shotty vesicles appeared on both feet, on the soles, between the toes and on the toes. The patient had to be hospitalized during this entire time, and a day and a night nurse were in attendance. The continued appearance of new lesions and the marked and increasingly severe pruritus long after the offending substance had been removed not only tended to make the patient skeptical, but would have made us doubt the correctness of our etiologic diagnosis had not the patch test been convincing. The site of this test continued to present an intense reaction for more than two weeks.

On August 18, all the areas began to improve, and from then on progress was gradually upward, with occasional returns of severe itching. The hands and feet desquamated with large lamellar scales, such as are seen in typical scarlet fever desquamation.

Patch Tests.—One and one half years after the eruption, we were able to make patch tests with the following substances: (1) butesin solution (1 per cent in

alcohol), (2) butesin picrate ointment (1 per cent) and (3) picric acid (saturated solution).

While the skin reacted alarmingly to all three preparations within twenty-four hours, the picric acid site showed such a severe grade of reaction that intensive treatment had to be instituted. After forty-eight hours, the entire arm was swollen. The appearance of the reactions was again of interest:

1. Butesin solution produced scattered follicular vesicles and papules larger than a pinhead, deep edema and little redness.

2. Butesin picrate ointment produced marked erythema and vesiculation, with some swelling.

3. Picric acid (saturated solution) produced an excessively strong reaction, with angry redness, swelling, vesiculation and a tendency to spread beyond the patch area.

The reactions took more than two weeks to subside, during which the entire arm remained swollen, and the patient became angry, as was justifiable in view of the great discomfort.

CASE 4.—Mrs. R. de M., 25 years old, in her seventh month of pregnancy, was referred to us by Dr. I. C. Rubin on Jan. 12, 1932, because of severe and persistent swelling of the vulva and clitoris, with severe itching which had spread to the upper part of the thighs, pubes and perineum. Besides the swelling and pruritus, there was a mild dermatitis of the inner aspect of the thighs, adjacent to the vulva. The patient also had a few small, broken vesicles on the interdigital webs of the hands.

Her history revealed that four months before consulting us, she had slight itching of the vagina and vulva, for which she used a 1 per cent butesin picrate ointment. This relieved the pruritus and she discontinued its use after three or four days. Although she had occasional slight recurrences of itching, she had employed other remedies (solution of aluminum acetate, N. F., and similar preparations) until four days before consulting us. She then again applied the butesin picrate ointment repeatedly, both in the vagina and on the vulva. Severe itching, swelling and dermatitis appeared. We made a patch test on the right thigh (normal skin) with a 1 per cent butesin picrate ointment. The reaction was positive after twenty-four hours, there being marked edema, accentuation of the follicular orifices (swelling of these areas, which gave an appearance like gooseflesh) and slight erythema. This reaction increased in severity and became intensely pruritic. It healed with slight scaling in about three weeks.

The further course of the eruption and of the pruritus is of interest. While the dermatitis on the thighs and the swelling of the vulva gradually subsided under local treatment, severe pruritus developed over the entire body. This was often excessive, and for more than a week the patient had little sleep, even though she employed sedatives. After four weeks, she could be discharged, although there was still a slight generalized pruritus. She refused to permit further testing at that time.

Comment.—In both case 1 and 2, it could be shown that the first signs of dermatitis did not appear until from one week to thirteen days after the butesin picrate ointment was last employed, and yet the patch tests showed a reaction within from twenty-four to forty-eight hours. The period of from one week to thirteen days is therefore not the lapse of time necessary between the contact and the appearance of the reaction, such as one frequently sees in delayed reactions (for

instance, in certain patch tests with trichophytin, in which it takes from three to four days or more for the reactions to develop, or in a case of procaine hypersensitiveness in which in repeated tests the reaction always became positive after forty-eight hours, being negative when the patch was first removed after twenty-four hours). In such cases of delayed reactions, the reaction time appears to be constant; at least repetition of the tests has always led to the same result. Moreover, the period between the cessation of the use of the ointment and the appearance of the dermatitis in our first two cases cannot be of the same character as that which is seen in sensitizations which appear only after the patient has been in contact with the offending substance for months or years. In the latter cases, the eruption frequently appears without cessation or interruption of contact. The patients are immune for some time and then, for a reason as yet unexplained in most cases, they become sensitized.

We should rather interpret the phenomenon in our cases as the *incubation period of sensitization* in patients who have come in contact with the drug probably for the first time. This period of incubation has striking similarities with that in other sensitizations, for instance, in serum disease and in experimental drug and plant sensitizations in animals. The appearance of the dermatitis from six to thirteen days after the cessation of contact corresponds almost exactly with the flare-up described by Frei [6] and by one of us (Sulzberger [7]) in arsphenamine sensitizations, and the explanation is probably the same. The mechanism is probably as follows: The intimate contact starts the sensitizing process, which develops gradually, the sensitivity reaching a certain degree after from six to thirteen days. At the end of this time, there is presumably still sufficient excitant present at the site of the application to act as a precipitating agent, and it is with this residual excitant (*Restantigen*) that the now hypersensitive cells react. (For a more detailed discussion of this phenomenon, see Sulzberger.[7])

There are thus three different periods representing three separate types of phenomena or phases in sensitizations of eczematous type:

1. *A period of refractoriness to sensitization*, which may last days, weeks, months or years, in which the patient is refractory to sensitization, in spite of intimate, often daily contact with a substance which may later sensitize.

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6. Frei, W.: Ueber willkürliche Sensibilisierung gegen chemisch definierte Substanzen: I. Untersuchungen mit Neosalvarsan am Menschen, Klin. Wchnschr. **7**:539, 1928.

7. Sulzberger, M. B.: Hypersensitiveness to Arsphenamine in Guinea-Pigs: I. Experiments in Prevention and in Desensitization, Arch. Dermat. & Syph. **20**:669 (Nov.) 1929; II. Experiments Demonstrating the Rôle of the Skin, Both as Originator and as Site of Hypersensitiveness, ibid. **22**:839 (Nov.) 1930.

2. *A period of incubation of sensitization,* which is the time required for sensitization to develop in a susceptible patient after he comes in contact with the sensitizing agent. The incubation of sensitization seems to be relatively constant for different substances, being approximately the same in our cases of butesin picrate dermatitis as it has been found to be in serum sickness, arsphenamine hypersensitiveness and other conditions.

3. *A period of development of reaction,* which may last minutes, hours or days, which is the period required for the reaction to become manifest after contact with a substance to which the patient has, at some previous time, become sensitized. The reaction time seems to be constant in a given patient and to a given excitant, and it is usually from sixteen to forty-eight hours.

We believe that the consideration of the incubation period explains the sparing of the sites of the burns in cases 1 and 2. Both of these burns destroyed the epidermis to a great extent, so that the epidermal covering of the burned area may be assumed to have been of new growth. As the application of ointment was discontinued after several days, the new epidermal cells did not have intimate or prolonged contact with butesin picrate. It is to be assumed that these new cells became sensitive to butesin picrate at the same time as all the other cells of the skin, for both these sites and distant areas of the skin reacted within twenty-four to forty-eight hours when a patch test was applied. But just as far distant skin areas, though equally sensitive, did not react until a new application was made, so these newly formed cells covering the burned area did not react—and apparently for the same reason. The newly formed hypersensitiveness encountered no excitant or insufficient excitant with which to enter into reaction. Just as in the distant skin areas, there had not been any, or at least not sufficient, contact of these new epidermal cells with butesin picrate, presumably because the applied ointment had been thrown off with the damaged epidermis and insufficient residual excitant remained at this site to cause a reaction.

We believe that this is the most logical conception of what occurred, and that it may be regarded as an added proof of the localization of the eczematous type of hypersensitiveness in the epidermis or, at least, in the most superficial parts of the skin.

Another observation of interest in our four cases is that two of the three patients we were able to test were sensitive to both butesin and picric acid (cases 2 and 3), whereas the third patient (case 1) was sensitive to butesin alone. This suggests that the application to a burned area (injured area) may constitute a situation peculiarly favoring sensitization. This seems to be the most adequate explanation of the fact that two patients became sensitized to two different and unrelated substances simultaneously. The supposition seems untenable that this was a group sensitivity, such as, for instance, the group sensitivity

shown in the reaction of the patient in case 1 to butesin and to ethylaminobenzoate, or the group sensitization that we have seen to the various arsphenamines, to the various mercurials or to the various chemicals of the procaine series. Case 1 seems to disprove this, for the patient reacted to butesin but not to picric acid. In this connection, we must recall the many cases in which trauma favoring the entrance of excitants has preceded sensitization. We must also mention the theory of complex antigens which may be applicable; the destroyed protein combines with the simpler chemical, butesin picrate, the former acting as the "*Schlepper*," or the larger, nonspecific carrier molecule, and the latter, as the smaller, but specific hapten (Landsteiner and Simms [8]).

It is further noteworthy that the two chemicals, butesin and picric acid, caused different types of reaction. The first elicited a response which was mainly follicular (similar to many trichophytin and tuberculin patch test reactions), which was accompanied by marked edema and pruritus and very little erythema, and which lasted for an astonishing length of time (several weeks). The second caused a diffuse, often severe erythema, little infiltration and very numerous, minute, nonfollicular vesicles, which desquamated and healed more speedily (fig. 2). These types of reaction were so consistent in the first three cases that we cannot but consider them as to some degree typical of the respective drugs. This being the case, we venture to predict that the patient in case 4, in whom the reaction to butesin picrate ointment was of the follicular and edematous (butesin) type, will certainly be found to be sensitive to butesin, and perhaps even to this drug alone.

The long duration of the eruption, with the continued appearance of new lesions in areas far from the application and after the discontinuance of the use of the drug, the generalized pruritus and the deep-seated, shotty, dermatophytid-like vesicles appearing even on the soles of the feet make it probable that there was a hematogenic distribution. This being the case, we have examples of dermatitis venenata at the site of application and dermatitis medicamentosa following absorption and hematogenic distribution to distant parts. Case 4 is of particular interest in this respect, as the dermatitis was negligible and the main symptom of severe pruritus affecting the whole body was probably due to absorption through the mucous membrane and subsequent distribution. We believe that such cases demonstrate the possibility of pruritus without cutaneous manifestations, having as its cause the blood-borne drugs or other harmful agents which may give rise to itching without clinically visible dermatitis. We have here, in other words,

8. Landsteiner and Simms: Production of Hetero-Genetic Antibodies with Mixtures of the Binding Part of the Antigen and Protein, J. Exper. Med. **38**:127, 1923.

a *dermatitis medicamentosa without dermatitis.* This type of itching is probably comparable to the pruritus occurring in diabetes, to that caused by the circulating bile acids in icteric conditions, and perhaps even to that known as senile pruritus.

The characteristics of (1) dissemination to distant parts, (2) severe pruritus without much dermatitis and (3) a dishearteningly protracted course seem to be encountered frequently in cases of dermatitis due to chemicals possessing local anesthetic properties. We have observed these characteristics in cases of dermatitis due to procaine hydrochloride, nupercaine and to lead and opium wash. It occurs to us that the reaction between these substances and the sensory nerves may explain the severe and persistent itching (Sulzberger and Kerr [9]).

CASES OF DERMATITIS DUE TO OTHER DRUGS

We now leave the cases of butesin picrate dermatitis, which we have found so instructive, and turn to several observations in cases due to other drugs. Many of these further observations have marked analogies with and are confirmatory of some of our observations on butesin picrate sensitization.

The following two cases again demonstrate the possible existence of dermatitis medicamentosa due to topical remedies, that is, absorption and distribution of a drug not following ingestion, or injection, but resulting from local application.

CASE 5.—Mr. S. R., aged 40, applied a proprietary ointment containing iodine to a small infection in a hair follicle on the right side of the neck. Only one application was made, to an area not over 1 inch (2.5 cm.) in diameter. Several hours later, a macular rash appeared on the legs, and the next day the face, scalp and entire body were covered with a macular and papulopustular eruption. The eruption was so severe that a tentative diagnosis of smallpox was made by another dermatologist. The condition lasted ten days and at the beginning was accompanied by a slight rise in temperature. *There was no dermatitis at the site of application.* The patient had used iodine previously without ill effect. He refused to permit testing.

CASE 6.—W. L., aged 33, applied a standard solution of mercurochrome to an open boil on the left forearm. After six days, the area of application presented an erythematous and vesiculating dermatitis, while the face, neck, shoulders and upper parts of the arms were covered with a morbiliform, noneczematous, bright red exanthem, and the sides of the torso presented numerous scattered, faint roseola-like macules. This rash gradually subsided and had disappeared by the end of ten days. Patch tests were positive, with eczematous reactions and vesicles at the sites of application of a standard solution of mercurochrome, of 1:1,000 solution of corrosive mercuric chloride and of a 5 per cent ammoniated mercury ointment.

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9. Sulzberger and Kerr: Sensitizations of Eczematous Type, J. Allergy **4**:326 (May) 1933.

We have seen two other cases of mercurochrome dermatitis, and a third and very severe case was called to our attention by Dr. Wilbert Sachs (reported by Pascher and Silverberg [10]).

CASES 6 and 7.—While the "immune" zone in these cases cannot be considered in any way analogous to the absence of dermatitis observed on the previously burned areas in cases 1 and 2, the cases presented phenomena of absorption through the skin and resulting dermatitis medicamentosa, as well as a puzzling "immunity" of the area of most intimate contact with the drug. In both cases a belladonna plaster had been applied. After the plaster had remained in place for several days, an erythematous, scarlatiniform and morbilliform eruption appeared on the areas surrounding the plaster and gradually spread until it covered practically the entire body. On removal of the plaster, we were astonished to find that the skin beneath it, which we had expected to be most severely affected, showed no vestige of eruption. The lesions stopped abruptly at the margins of the site which had been covered. At no future time did any lesions develop within this area of normal skin. We have no explanation to offer, but wish merely to call attention to the fact that J. Jadassohn [4] reported a case of sensitiveness to mercury in which an area which had been covered by a mercurial plaster, and which had previously reacted with a dermatitis, remained free from eruption when, some time later, an injection of mercury caused a generalized eczematous dermatitis affecting the rest of the skin.

SUMMARY AND CONCLUSIONS

While there is no method of testing which has proved generally satisfactory in fixed drug eruptions and in many other forms which have no typically eczematous component, in the truly eczematous type of dermatitis caused by drugs the contact or patch test is of value.

We were able to study four cases of hypersensitiveness to butesin picrate ointment in which the eruption was a dermatitis eczematosa and in which the epidermis gave positive reactions to patch tests. Our study brought the following facts to light:

1. In two cases it could be shown that clinical evidence of sensitization developed in from one week to thirteen days after the use of the medicament was discontinued. This period of sensitization is analogous to that observed in sensitizations to serums, to arsphenamine and other drugs and to plants. We were able, therefore, to distinguish three distinct phases or periods in sensitizations of an eczematous nature:

(*a*) A period of refractoriness to sensitization, during which the patient's skin does not become sensitized, in spite of intimate contact with a substance which may at some later time and for some unknown reason suddenly cause a sensitization. The length of this period varies from days to years. (*b*) A period of incubation of sensitization, which is the time required for sensitization to develop in a patient coming in contact with a sensitizing agent during a state of susceptibility to

10. Pascher and Silverberg: Hypersensitivity to Mercurochrome Shown by the Patch Test, Arch. Dermat. & Syph. **27**:408 (March) 1933.

sensitization. In the cases that we have observed, this seems to be relatively constant, independent to some degree of both patient and excitant. The usual time in most sensitizations, whether to drugs, to plant products or to foreign serums, is approximately from one to two weeks in both human beings and animals. (*c*) A period of development of clinically manifest reaction, which is the time elapsing between contact with the excitant and the appearance of the clinical reaction in an already hypersensitive patient. This period varies from hours to days (usually being from sixteen to forty-eight hours) and seems constant in a given patient with a given excitant.

2. In two cases in which butesin picrate ointment had been applied because of burns which had to a great degree destroyed the epidermis, the subsequent dermatitis affected the area surrounding the site of the burn and not the new epidermis covering the burned area. Nevertheless, the new and nonaffected epidermis was not immune, as it reacted within twenty-four hours to subsequent patch tests with butesin picrate. These observations are best explained as follows: At the time of the first applications of butesin picrate ointment, the new epithelial covering of the burned sites had not been entirely formed and had had, therefore, little or no contact with the excitant, which had been carried off with the injured and desquamating cells. When the new cells of this area became hypersensitive in due course, there was not sufficient excitant present at the site to precipitate the reaction (theory of reaction with residual excitant). However, when butesin picrate was later reapplied to this area, the newly formed and sensitized cells reacted in the same manner as any far-distant areas which had had no previous contact with the excitant.

3. In two cases, patch tests showed that the patients were hypersensitive to both butesin and picric acid; in a third case, the patient was hypersensitive to butesin but not to picric acid. As three of the sensitizations followed application to denuded, burned areas, and as two of the patients became simultaneously sensitized to two chemically unrelated substances (butesin and picric acid), it is to be assumed that trauma of this type peculiarly favors sensitization (hapten plus protein as full antigen [Landsteiner]).

4. In the patients found to be hypersensitive both to butesin and to picric acid it could be noticed that each of these substances seemed to have an individual, specific, more or less typical and characteristic reaction. Butesin caused a persistent follicular eruption and deep edema, with little redness; picric acid, on the other hand, caused diffuse, severe erythema, little edema and many minute nonfollicular vesicles. The test sites reacting to butesin picrate ointment in patients sensitive to

both the components presented the picture of a combination of the butesin and the picric acid types of reaction.

5. The long duration of the eruptions in some of our cases, the continued new appearance of fresh lesions at distant points and the severe and intractable pruritus which became generalized and lasted for many weeks after cessation of contact with the offending substance lead us to believe that in some of these cases we were dealing both with a dermatitis venenata, due to external contact, and with a dermatitis medicamentosa, due to absorption and hematogenic distribution. We cited two further examples of this combination: one due to iodine and the other to mercurochrome. These observations lead to two practical conclusions, as follows: Pruritus without visible manifestations may be due to the dissemination of drugs, in other words, a sort of "dermatitis medicamentosa without dermatitis"; and dermatitis medicamentosa not only may follow ingestion or injection, but may result from local application.

6. Two further cases were briefly described of dermatitis medicamentosa due to local application of a belladonna plaster and absorption of the drug through the skin. In both these cases, we noted the astonishing fact that the area which had been occupied by the plaster, and in the most intimate contact with the harmful agent, remained unaffected.[11]

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11. For all further references concerning skin sensitizations of various types, see Jadassohn, W.: Die Immunbiologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2.

COLLOIDAL MERCURIC SULPHIDE

CLINICAL STUDY

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New therapeutic agents are often endowed at the time of their induction with striking curative virtues that later prove illusive. Time, braced by the accumulated experience and impartial criticism of clinicians, leaves few to weather the storm. The seriousness of syphilis and the limitations of the present therapeutic armamentarium have kept chemists and physicians constantly on the alert for something more destructive to the causative organism and less dangerous to the host. For this reason, there is now a swing to colloidal drugs, in the hope that, owing to the finer division of particles and the resultant higher dispersive phase, an increase in therapeutic effect will be obtained.

Syphilis has proved itself very resistant to the attainment of a perfect therapeutic score by any agent, and mercuric sulphide has not been able to establish a classic position in this respect.

In order to establish the real value of this chemical compound, and to note some of its effects, I selected a few cases of syphilis representing the infection in its various manifestations (table 1) and used the drug both intravenously and intramuscularly. To give a detailed report of each case would be interesting but impracticable. I shall therefore offer only the outstanding effects of the therapy as manifested clinically.

Mercuric sulphide (Hg S)) is a combination of 86.22 per cent metallic mercury and 13.78 per cent sulphur (manufacturer's statement). It is prepared by what is known in colloidal chemistry as the "condensation method" and stabilized by a specially prepared hydrolized denatured protein. It is a dark brown solution, noncorrosive, freely soluble in water and available in two strengths, 1 and 2 per cent. The solution seems remarkably well stabilized; on standing for one year it showed no change in chemical composition or in gross precipitates.

From the Department of Dermatology and Syphilology, Northwestern University Medical School, service of Dr. Arthur W. Stillians.

This work has been made possible through the cooperation of our own technician, Miss Bertha Culka, the clinical laboratory of the University and Dr. Henry Joseph Zettleman, who gave unstintingly of his time and thought to the work at hand.

TABLE 1.—*Effect of the Injection of Colloidal Mercuric Sulphide on the Wassermann and Kahn Reactions of the Blood of Persons with Syphilis*

		Blood									
		Before		After 12 Injections		After 24 Injections		After 36 Injections		1 Month or More After	
Case	Diagnosis	Wassermann	Kahn	Wassermann	Kahn	Wassermann	Kahn	Wassermann	Kahn	Wassermann	Kahn
1	Gumma	4+	3+	4+	4+	4+	4+ Changed to neoarsphenamine				
2	Tabes	Neg.	Neg.	Neg.	Neg.	Neg.	2+	Neg.	2+	Neg.	Neg.
3	Tabes	Neg.	2+	2+	3+	Neg.	2+	...	...	Neg.	Neg.
4	Gumma	3+	3+	Neg.	3+	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
5	Latent syphilis	2+	4+	Neg.	4+	...	...	...	...	...	...
6	Tabetic form of dementia paralytica	3+	2+	4+	2+	2+	Neg.	...	...	3+	Neg.
7	Tabetic optic atrophy	4+	2+	4+	4+	4+	4+	4+	3+	4+	3+
8	Latent syphilis	3+	2+	3+	3+	...	...	4+	2+	Neg.	Neg.
9	Cerebral syphilis	4+	3+	3+	2+	...	...	...	...	...	...
10	Secondary syphilis	4+	4+	4+	4+	4+	4+	...	...	After 9 injections of neoarsphenamine	
11	Tabes	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+
12	Latent syphilis	4+	3+	2+	2+	Neg.	2+	Neg.	Neg.	Neg.	Neg.
13	Secondary chorioretinitis	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
14	Latent syphilis	4+	4+	4+	4+	Neg.	4+	...	...	...	...
15	Latent syphilis	4+	4+	4+	4+	2+	2+	3+	2+	3+	Neg.
16	Latent syphilis	Neg.	3+	Neg.	3+	Neg.	Neg.	...	...	Neg.	Neg.
17	Gumma	4+	4+	2+	4+	Given 10 injections of neoarsphenamine				Neg.	3+
18	Iritis	3+	2+	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
19	Primary syphilis	4+	3+	4+	4+	Given combined neoarsphenamine and colloidal mercuric sulphide Discontinued treatment; returned after 3 mos. with florid secondary lesions					
20	Dementia paralytica	4+	4+	4+	3+	4+	3+	4+	3+	4+	2+
21	Gumma	4+	3+	4+	3+	4+	3+	...	...	...	...
22	Secondary iritis	4+	3+	4+	3+	Discontinued					
23	Gumma	4+	2+	4+	3+	4+	4+	...	...	4+	Neg.
24	Gumma	4+	4+	4+	4+	3+	3+	...	...	...	...
25	Dementia paralytica	4+	4+	4+	3+	4+	4+	...	...	...	...
26	Aortitis	4+	3+	3+	3+	...	...	...	...	...	...
27	Gumma	4+	4+	4+	4+	...	...	...	...	...	...
28	Nerve deafness	4+	4+	4+	4+	4+	3+	2+	1+	3+	3+
29	Gumma	4+	4+	4+	4+	4+	3+	...	...	...	...
30	Secondary syphilis	4+	4+	4+	4+	4+	4+	Neg.	Neg.	4+	3+
31	Latent syphilis	4+	2+	3+	1+	2+	3+	...	...	2+	3+
32	Latent syphilis	3+	4+	2+	4+	...	...	...	...	...	...
33	Latent syphilis	3+	2+	7 injections of drug discontinued							
34	Latent syphilis	4+	Neg.	4+	1+	Neg.	Neg.	...	...	Neg.	Neg.
35	Gumma	3+	2+	2+	2+	Discontinued					
36	Latent syphilis	4+	4+	4+	4+	4+	4+	...	...	4+	3+
37	Tabetic form of dementia paralytica	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+
38	Vascular syphilis	4+	4+	4+	4+	3+	3+	...	...	...	...
39	Secondary iritis	4+	2+	4+	2+	...	...	...	...	...	...

The dosage which I used was 3 cc. twice weekly, except when 4 cc. was used in an effort to prove the value of the administration of an alkali. I have arbitrarily chosen 12 injections as a course.

The effect of this therapy on the Wassermann reaction was given primal importance. As noted in tables 1 and 2, a Wassermann and a

TABLE 2.—*Effect of Injections of Colloidal Mercuric Sulphides on the Spinal Fluid of Persons with Syphilis*

		Before					One Month or More After Treatment				
			Globulin Nonne					Globulin Nonne			
Case	Diagnosis	Wassermann	Phase 1	Phase 2	Cells	Colloidal Gold Reaction	Wassermann	Phase 1	Phase 2	Cells	Colloidal Gold Reaction
1	Gumma										
2	Tabes	3, 4+	Neg.	Neg.	4	11122210000	Neg.	0	0	0	00000000000
3	Tabes	4+	.....	.....	..	.....	Neg.	0	0	1	00000000000
4	Gumma										
5	Latent syphilis										
6	Tabetic form of dementia paralytica	4+	Strong	Strong	39	44444321000	3, 4+	Neg.	Neg.	4	55544210000
7	Tabes, optic atrophy	4+	Strong	Strong	68	00123444440	4+	Slight	Slight	45	0013321000
8	Latent syphilis	Neg.	Neg.	Neg.	2	00121000000	Neg.	Neg.	Neg.	2	0000000000
9	Cerebral syphilis	Neg.	Neg.	Neg.	..	00000000000	Neg.	Pos.	Pos.	35	4322100000
10	Secondary syphilis	2+	.....	.....	..	.....	3+				
11	Tabes	4+	Neg.	Neg.	2	0001232100	4+	Neg.	Neg.	1	1233100000
12	Latent syphilis	Neg.	Neg.	Neg.	7	0000000000					
13	Secondary syphilis	Neg.	Neg.	Neg.	3	01112110000	Neg.	Neg.	Neg.	4	000000000
14	Latent syphilis										
15	Latent syphilis	3, 2+	Neg.	Neg.	2	0001110000					
16	Latent syphilis	Neg.	Neg.	Neg.	6	1111000000					
17	Gumma										
18	Iritis										
19	Primary syphilis										
20	Dementia paralytica	4+	Strong	Strong	200	5555554110	4+	Pos.	Pos.	30	55554321000
21	Gumma	Neg.	Neg.	Neg.	3	0012342100					
22	Iritis										
23	Gumma	Neg.	Neg.	Neg.	3	0000000000					
24	Gumma	Neg.	Neg.	Neg.	1	1111100000					
25	Dementia paralytica	4+	Strong	Strong	20	5555432100	4+	Pos.	Pos.	30	5555443200
26	Aortitis										
27	Gumma										
28	Nerve deafness	4+	Neg.	Neg.	4	1233444210	2+				
							4+	Neg.	Neg.	2	0000000000
29	Tertiary syphilis	Neg.	Neg.	Neg.	2	0000000000	Neg.	Neg.	Neg.	2	
30	Secondary syphilis										
31	Latent syphilis	Neg.	Slight	Neg.	4	0000000000	Neg.	Neg.	Neg.	2	
32	Latent syphilis										
33	Latent syphilis										
34	Latent syphilis										
35	Gumma										
36	Latent syphilis	4+	Strong	Strong	73	1233455550	Neg.	Neg.	Neg.	1	00001100000
37	Tabetic form of dementia paralytica										
38	Vascular syphilis										
39	Iritis, secondary syphilis—1. Positive in 2 cc. 2. Positive in 5 cc. 3. Positive in 2 cc.										

Kahn test were done both on the blood and on the spinal fluid before each course of injections and again one month or more after the cessation of treatment. Of thirty-nine treated patients, thirty-seven had positive Wassermann tests of the blood. At the end of one course (twelve injections), one of the positive reactions had changed to negative. At the end of twenty-four injections, four had changed to negative.

Thirteen of the patients received thirty-six injections, and still only four negative reactions were found. One month or more after the cessation of treatment, twenty-three Wassermann tests were made, and of these seven were negative. The serologic results show an ability of this therapy to alter the Wassermann reaction in a sizable percentage of cases immediately after the termination of treatment and in a slightly greater percentage a month or more later. This shows an ability of the human organism to store the chemical product and the beneficial effects due to its gradual release. The patients in cases 2 and 13 were used as controls to find the effect of the therapy in cases in which a negative reaction had been obtained by previous treatment with neoarsphenamine, bismuth and iodides. Table 2 gives the effect of this treatment on the spinal fluid. Before treatment the spinal fluids of twenty patients were subjected to the Wassermann test, the colloidal gold test, the globulin test and cell counts. The spinal fluids of ten of these twenty patients gave positive reactions. One month or more after the cessation of treatment the spinal fluids of fourteen patients were subjected to a second test, and eight gave negative reactions. But of these eight, four gave negative reactions before treatment was instituted. Case 9 is especially to be mentioned because the second test revealed an increase in globulin and a decided change in the colloidal gold reaction. Four of the nine cases in which there was a strong positive Wassermann reaction before treatment showed serologically a decided change toward betterment. One could say from these figures that in syphilis of the central nervous system the drug gives promise of high therapeutic value. Its chief effect was a reduction of the number of cells and a lessening of the globulin content of the spinal fluid. Three cases in this series, 2, 3 and 36, were exceptions to this observation, the reaction of the spinal fluid changing completely from positive to negative. Parenchymatous syphilis of the central nervous system proved just as resistant to this form as to inorganic mercury.

In two cases of primary syphilis the results were too slow to permit continuance of the treatment. In one, spirochetes were present after five injections; in the second, spirochetes were still present in the regional glands after seven injections. In the face of this, I could not sacrifice a patient on the altar of scientific investigation, losing an opportunity to prevent generalization of the infective organisms. So all other persons with primary lesions were given a combination, neoarsphenamine and mercuric sulphide. For this reason I cannot offer any specific data on the amount of the preparation necessary to sterilize chancres.

Colloidal mercuric sulphide cannot be compared to arsphenamine in its ability to render moist early lesions noninfectious.

The kidneys are very sensitive to the action of mercury. Table 3 shows the effect of colloidal mercuric sulphide on the renal apparatus. The renal function of thirty-nine patients was studied before treatment was instituted. The urine of all except one was negative for albumin and casts. Ten of the patients had no excretory deficiency as shown

TABLE 3.—*Effect of Colloidal Mercuric Sulphide on the Renal Apparatus of Persons with Syphilis*

		Before				After				One Month or More After Cessation of Treatment			
					Per Cent of Dye				Per Cent of Dye				
Case	Diagnosis	Albumin	Casts	Total Cc. of Urine	Excreted	Total Cc. of Urine	Excreted	Albumin	Casts	Total Cc. of Urine	Excreted	Albumin	Casts
1	Gumma	0	0	610	75	95	71	0	0				
2	Tabes	0	0	...	..	288	30	0	0	105	64	0	0
3	Tabes	0	0	...	..	115	90	0	0				
4	Gumma	0	0	...	..	40	10	+	+	240	80	+	+
5	Latent syphilis	0	0	...	..	550	67	0	0	720	92	0	0
6	Tabetic form of dementia paralytica	0	0	54	77	220	33	+	+	230	72	0	0
7	Tabes, optic atrophy	0	0	...	..	139	78	+	+	285	52	+	+
8	Latent syphilis	0	0	260	70	152	67	0	0	205	78	0	0
9	Cerebral syphilis	0	0	...	..	145	62	0	0				
10	Secondary syphilis	0	0	375	75	72	58	0	0				
11	Tabes	+	+	...	..	113	15	+	+	320	45	+	+
12	Latent syphilis	0	0	...	..	150	75	0	0				
13	Secondary syphilis	0	0	...	..	70	72	0	0	790	73	0	0
14	Latent syphilis	0	0	134	80	85	25	+	+	50	75	+	+
15	Latent syphilis	0	0	266	75	160	4 5	0	0	172	68	0	0
16	Latent syphilis	0	0	455	55	335	53	0	0				
17	Gumma	0	0	132	90	662	57	0	0				
18	Iritis	0	0										
19	Primary syphilis	0	0	...	..	315	60	0	0				
20	Dementia paralytica	0	0	...	..	110	75	0	0	...	..	0	0
21	Gumma	0	0	...	..	180	70	0	0				
22	Iritis	0	0	153	72								
23	Gumma	0	0	...	..	89	55	0	0	55	37	0	0
24	Gumma	0	0	...	..	200	75	0	0				
25	Dementia paralytica	0	0	...	..	...	..	0	0	...	..	0	0
26	Aortitis	0	0	...	..	...	..	0	0				
27	Gumma	0	0										
28	Nerve deafness	0	0	...	..	68	80	0	0				
29	Gumma	0	0	...	..	...	..	0	0				
30	Secondary syphilis	0	0	580	73	200	60	0	0				
31	Latent syphilis	0	0	...	..	220	93	0	0	298	92	0	0
32	Latent syphilis	0	0										
33	Latent syphilis	0	0										
34	Latent syphilis	0	0	...	..	...	..	0	0				
35	Gumma	0	0										
36	Latent syphilis	0	0	...	..	253	60	0	0	130	52	0	0
37	Tabetic form of dementia paralytica	0	0	...	..	360	81	0	0				
38	Hemiplegia	0	0	...	..	...	..	0	0				
39	Secondary syphilis	0	0	...	..	325	30	4+	4+	3	..	+	+

by the phenolphthalein test. Immediately following cessation of treatment, six of thirty-four patients tested showed signs of renal irritation, albumin and casts. Twenty-eight were tested for renal function at this time. Of these, six showed a percentage of less than 40, which I have used as the lower limit of normality. But of the ten patients tested before treatment, six showed a marked reduction in the percentage of dye excreted. Besides the especially noticeable percentage of patients in whose urine the presence of albumin and casts was noted is the still

higher percentage in whom there was an appreciable lowering of the excretory function as shown by the dye test. After a period of rest the excretory level was reestablished without any apparent permanent residual injury. The impression obtained is that colloidal mercuric sulphide is a renal irritant of major importance. A reduction in excretory function is the first evidence. This offers a potent reason why each

TABLE 4.—*Changes in the Blood Before and After Treatment*

	Before							After						
	Total			Differential				Total			Differential			
Case	Hemoglobin	Red Blood Cells	White Blood Cells	Lymphocytes	Polymorphonuclears	Eosinophils	Basophils	Hemoglobin	Red Blood Cells	White Blood Cells	Lymphocytes	Polymorphonuclears	Eosinophils	Basophils	Others
1	75	4,720,000	14,050	30	69	1	..	90	5,350,000	11,100	15	77	..	1	3
2	..	.....	.....	..	..	..	..	90	5,250,000	7,700	33	66	..	..	1
3	80	4,930,000	10,350	26	72	1	1	88	6,400,000	13,258	22	78	..	..	..
4	80	4,810,000	13,550	19	75	6	..	80	4,900,000	7,200	28	72	..	..	..
5	70	4,840,000	4,180	34	66	..	..	75	5,000,000	6,600	24	74	..	..	..
6	75	4,700,000	7,700	31	67	2	2	80	4,380,000	5,900	40	57	..	2	..
7	85	4,100,000	5,750	28	70	1	1	80	4,780,000	7,500	41	59	..	..	..
8	90	5,880,000	6,600	12	87	1	..	85	5,440,000	7,800	31	68	..	1	..
9	..	.....	.....	..	..	..	..	..	.....	.....	..	..	..	..	..
10	80	4,700,000	9,050	26	74	..	..	..	.....	.....	..	..	..	..	..
11	80	4,880,000	12,600	20	80	..	..	90	4,610,000	8,750	25	73	2	..	..
12	85	6,020,000	12,300	26	73	1	..	75	5,990,000	5,500	42	58	..	..	..
13	..	.....	.....	..	..	..	..	75	5,180,000	11,100	29	70	1	..	..
14	..	.....	.....	..	..	..	..	73	5,100,000	9,000	36	59	4	1	..
15	80	4,610,000	7,100	41	56	1	2	80	4,790,000	7,750	29	68	2	1	..
16	80	5,020,000	8,950	34	66	..	..	80	3,670,000	9,050	27	72	1	..	..
17	85	3,170,000	5,000	40	60	..	..	85	5,470,000	12,950	34	58	6	2	..
18	..	.....	.....	..	..	..	..	..	.....	.....	..	..	..	..	..
19	95	4,950,000	5,400	..	..	..	..	90	4,880,000	6,600	40	56	2	..	2
20	..	.....	.....	..	..	..	..	85	4,630,000	8,400	20	79	1	..	..
21	..	.....	.....	..	..	..	..	70	4,320,000	6,850	30	68	1	1	..
22	75	.....	.....	23	72	2	3	..	.....	.....	..	..	..	..	..
23	80	4,900,000	9,100	17	80	1	2	75	4,610,000	12,550	21	65	2	2	..
24	80	5,370,000	6,350	50	50	..	..	85	4,720,000	7,500	30	70	..	..	..
25	Incomplete														
26	Incomplete														
27	Incomplete														
28	80	4,400,000	11,250	41	59	..	..	85	5,410,000	8,400	27	71	2	..	..
29	80	5,010,000	7,950	35	58	3	2	..	4,670,000	9,400	23	76	1	..	..
30	75	4,540,000	8,400	33	66	1	..	80	4,250,000	9,100	29	70	1	..	..
31	..	.....	.....	..	..	..	..	..	5,450,000	9,050	21	76	2	1	..
32	Incomplete														
33	Incomplete														
34	78	5,660,000	5,050	40	55	4	1	80	4,600,000	6,300	47	51	2	..	..
35	80	4,700,000	11,950	21	76	3	..	90	4,780,000	9,450	30	68	2	..	..
36	85	5,260,000	5,650	26	71	2	1	75	4,760,000	6,800	44	52	2	2	..
37	75	4,830,000	6,000	35	62	3	..	88	4,750,000	5,050	25	72	1	1	1
38	85	4,950,000	6,800	43	54	1	2								
39	80	5,290,000	18,100	13	86	1	..								
22	75	4,650,000	7,600	23	72	2	3								

syphilitic patient should receive a critical renal examination before, during and at stated intervals following mercurial therapy. The change of form has not altered the power of the mercurial agent.

Table 4 records the changes in the blood before and after treatment. A number of patients, even before treatment and without any other evident infectious process, presented a high leukocytosis. The majority of these patients showed a decided trend toward normality after mer-

TABLE 5.—*Clinical Results*

Case	Type and Location of Lesions	No. of Injections	Clinical Course	Complications
1	Gummas of right leg and hard palate	19	Oral lesions disappeared after 5 injections; lesion on leg persisted	Mercuric pigmentation at site of injection; persistence of lesion on leg
2	Tabes dorsalis with vomiting	36	Vomiting relieved for 1 year	Reduction of renal function
3	Tabes dorsalis	24	Improved	Gingivitis; muscular pains after 8 injections
4	Gumma of leg	36	Healed after 8th injection; potassium iodide used	Marked loss in weight; renal damage; no gingivitis
5	Latent syphilis	12	General health improved	None
6	Tabetic form of dementia paralytica	24	General health improved	None
7	Tabes; optic atrophy	37	No change	Renal damage
8	Latent syphilis	35	General health improved	None
9	Cerebral syphilis	12	General health improved	Increase of weight
10	Secondary syphilis	18	Moderate improvement after 17 injections	Gingivitis
11	Tabes; shooting pains	36	No improvement	Gingivitis; muscular soreness; loss in weight; renal damage
12	Latent syphilis	36	Generally improved	None
13	Secondary syphilis; chorioretinitis	36	Improved	None
14	Latent syphilis	24	.....	Stomatitis; renal damage
15	Latent syphilis	36	Generally improved	Gingivitis
16	Latent syphilis	24	Improved	Secondary anemia; potassium iodide used
17	Gummas in mouth and on lower extremities	14	Oral lesions cleared; others remained; treatment changed to neoarsphenamine	Renal damage
18	Syphilitic iritis	..	Combined neoarsphenamine and colloidal mercuric sulphide; marked general improvement	None
19	Primary syphilis	12	Lesion healed after 6 injections	Patient stopped treatment after 8 injections; returned in 3 mos. with secondary syphilis of 1 month's duration
20	Dementia paralytica	36	No improvement	None
21	Gumma; hard palate	27	Lesion healed after 9 injections	Gingivitis after 4 injections; typical mercuric exfoliative dermatitis
22	Syphilitic iritis	12	Iritis disappeared after 5 injections	Gingivitis
23	Gumma; scars only	24	Generally improved	Stomatitis after 9 injections
24	Gumma of neck	29	Generally improved	None
25	Dementia paralytica	19	Generally worse	
26	Aortitis	14	Generally improved	None
27	Gummas of legs	12	No improvement	Localized mercuric pigmentation
28	Nerve deafness	36	No improvement	None
29	Tertiary syphilis	20	Slight improvement in lesions	Gingivitis; marked loss in weight
30	Secondary syphilis	36	Rash disappeared after 11 injections	None
31	Latent syphilis	24	Generally improved	Mercuric pigmentation
32	Latent syphilis	13	Undetermined	None
33	Latent syphilis	7	Downgrade	Muscular soreness; marked gingivitis; loss in weight; dermal hemorrhages; pains in joints
34	Latent syphilis	18	Downgrade	Muscular pains; weakness; pains in joints; gingivities; marked loss in weight
35	Gumma	13	Improved	None
36	Latent syphilis	24	Physically better	None
37	Tabetic form of dementia paralytica; chorioretinitis	36	No change	Gingivitis
38	Hemiplegia	21	No change	Gingivitis
39	Syphilis; secondary iritis	8	Skin lesion improved after 3 injections; iritis after 7 injections	Gingivitis; renal irritation (table 4)

curialization. In several cases before and after treatment the eosinophilic and basophilic counts were noticeably high, and therefore were not influenced by this type of mercury.

In spite of the number of injections and the high dosage given, mercurial secondary anemia was observed only once; in case 16 secondary anemia developed. This type of mercury seems lacking in any special corpuscular toxicity.

Under the heading "Clinical Results," table 5, special emphasis has been placed on two factors: the effect of the mercury compound on the manifest lesion or lesions and the toxic effect of the drug. Of thirty-nine patients treated, twenty-three were improved either in general health or in some special manner; fourteen acquired complications involving mucous membrane, stomatitis or gingivitis. Although only three cases are cited in the tables, subsequent observations revealed that mercurial pigmentation had developed at the sites of injections in ten of the thirty-nine cases. Seven of the thirty-nine patients showed renal damage. Three of the thirty-nine had clinical syndromes typical of scurvy. Twenty showed some form of mercurial complication.

The sites of intramuscular and intravenous injections in a large percentage of patients assumed a deep-bluish discoloration. The sites of intramuscular injections were more prone to do this if there was a large amount of adipose tissue or if there was sclerosis from previous types of intramuscular injections. Roentgenograms, made from one to two months following the last injection, showed peculiar shadows which the laboratory reported as positive for metallic deposits. In intravenous therapy the bluish pigmentation is somewhat of an embarrassment, especially for women in wearing short sleeves. It can be prevented to a certain extent, but not absolutely, by the insertion of a detached needle. One must make sure that the needle is in the lumen of the vein and then attach the syringe. As shown by figures 1 and 2, this phenomenon is due to mercurial deposits in the superficial tissues.

These deposits are to be seen especially in the lower cell layers of the epidermis and scattered throughout the corium. The histiocytes as seen in the interfascicular spaces of connective tissue are engorged. As shown in figure 2, the deposits are especially heavy around the appendages. Figure 3 illustrates the long-continued presence of mercury in these bluish areas. Three months after the last injection of colloidal mercuric sulphide, a biopsy specimen was taken from the center of the area of discoloration shown by the large dark circle. Instead of alcohol as a cleansing agent, tincture of iodine was used. An intense inflammaory reaction occurred in and about the biopsy wounds, limited to the zone of bluish discoloration; on the opposite side, used as a control, no reaction occurred. A second patient was exposed to the same procedure with a similar result. The inference here is that a chemical reaction took

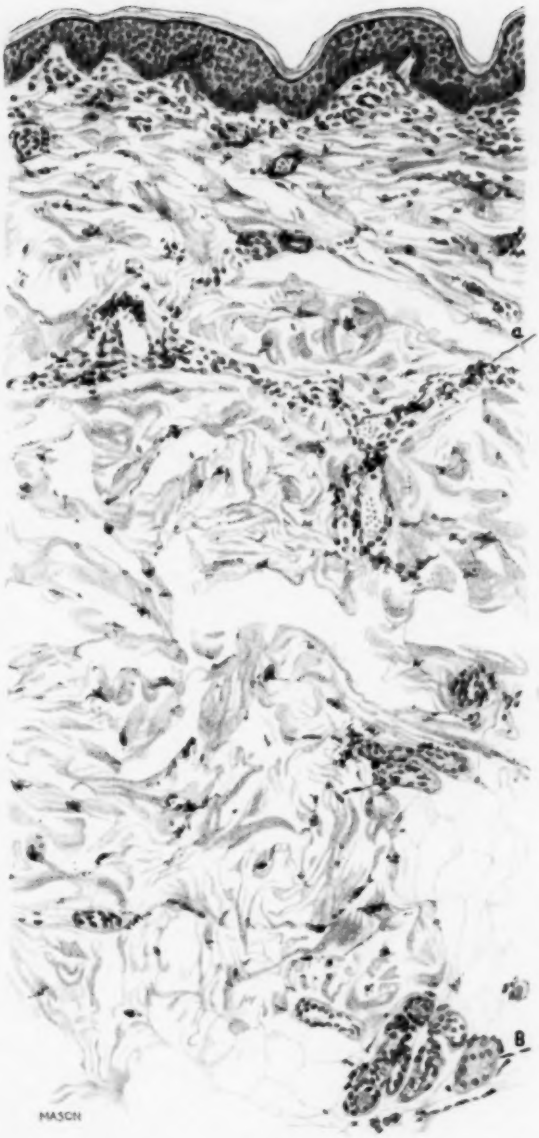

Fig. 1.—General view of an injected area, showing: *a*, pigmentation of the basal layer, lymphatic paths and around the glandular organs (*B*). This is due to the presence of mercury. The connective tissue shows evidence of moderate sclerosis and cellular infiltration of the upper dermis.

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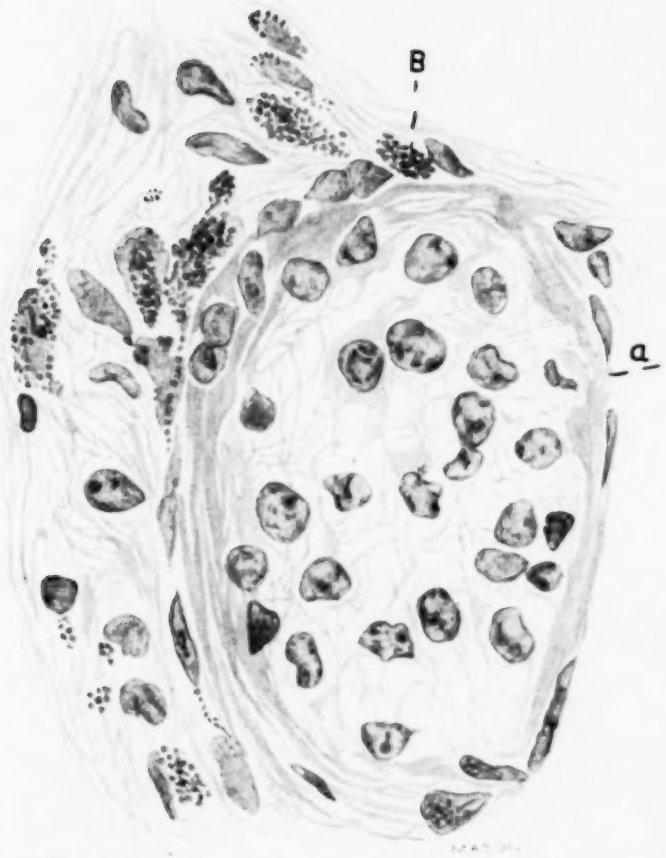

Fig. 2.—A higher magnification of *B* in figure 1; *a* shows the wall of the gland; *B*, mercury salts.

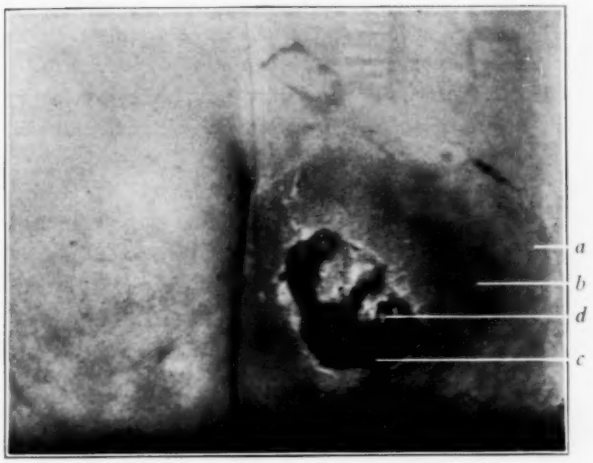

Fig. 3.—Hyperpigmentation following intramuscular injections. Reaction following the local use of tincture of iodine: *a*, mercurial hyperpigmentation; *b*, inflammatory zone; *c*, zone of dermal necrosis, and *d*, biopsy wounds.

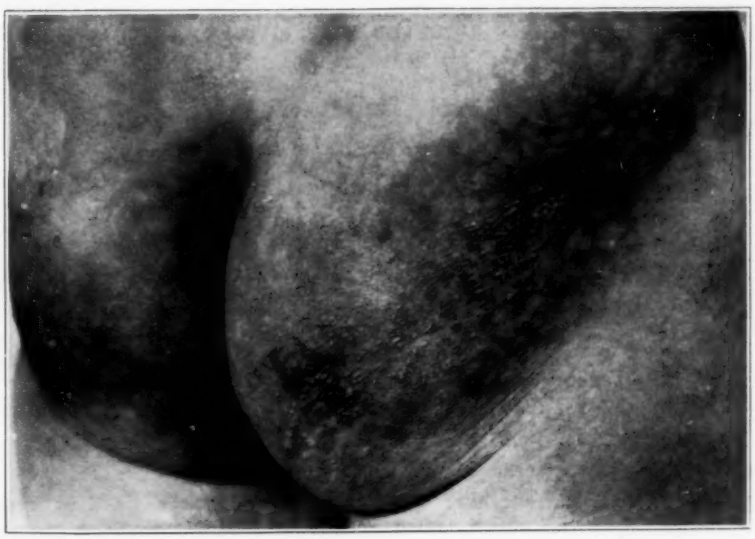

Fig. 4.—Dermatitis medicamentosa following the intramuscular injections.

place between the mercury in the tissue and the iodine to form the very irritating mercurous and mercuric iodide.

Figure 4 pictures a localized eruption consisting of deep red to purplish flattened papules, limited to the zone of injection. The lesions were elevated, circumscribed and infiltrated, and varied in size up to 2 mm. Some of the papules were umbilicated, each umbilication being at a follicular opening. The clinical picture was that of a patch of lichen planus, but histologically the arrangement of the cellular infiltrate was not typical. There was also a resemblance to herpes zoster, on account of the unilateral arrangement and the seeming tendency to follow a definite nerve distribution. Against this, however, was the lack of a deep boring pain and vesiculation. This is probably an atypical form of dermatitis medicamentosa. One patient (case 21) presented a generalized scarlatiniform eruption of moderate intensity. This was followed in two weeks by a mild exfoliation.

In table 6 are disclosed a marked frequency of gingivitis, an inherent tendency to renal irritation, and in three cases, the clinical syndrome of scurvy, that is, bleeding from the gums and into the skin, pains in the joints and loss of weight.

In table 5, under the heading of "Clinical Course," some interesting facts are noted: (1) Colloidal mercuric sulphide had a rapid effect on lesions of the mucous membranes and (2) the response of ulcerative lesions of the skin on the lower extremities was poor. This was probably due to the action of reversible chemical compounds in an area where hydrogen sulphide gases and bacteria were active. This result illustrates the need of local treatment.

The fact that the administration of mercury over a period of time leads to a marked fall in glycogen and in serum calcium and also to a greatly increased production of lactic acid suggests the administration of alkalis to patients as a part of the mercurial course or as an aid in the treatment of the complications. As shown in table 6, two types of alkali were employed, one containing acid sodium phosphate and sodium bicarbonate in equal portions; the second, an effervescent preparation of citrates and carbonates of calcium, sodium, potassium and magnesium. The latter was much more effective in curing and preventing the usual mercurial complications. Gingivitis and stomatitis were cured in all cases, but the treatment with alkali had no effect on the areas of mercurial pigmentation.

This investigation included: primary syphilis, one case; secondary syphilis, four cases; tertiary syphilis, ten cases; aortitis, two cases; nerve deafness, one case; iritis, three cases; chorioretinitis, two cases; latent syphilis, ten cases; cerebral syphilis, one case; tabes, four cases; tabetic form of dementia paralytica, one case; tabes with optic atrophy, one case, and dementia paralytica, two cases. (All the patients with

TABLE 6.—*Results Following the Administration of Alkali*

Case	Diagnosis	Complications Due to Mercuric Sulphide (Not Renal)	Effect of Alkali Therapy	Comment
1	Gumma	None	None	
2	Tabes	None	None	
3	Tabes	Pains in joints and muscles; dermal gingivitis; hemorrhages	Improved	Marked improvement on addition of fruits to diet
4	Tertiary syphilis	Gradual loss in weight	Good	Alkali given throughout course
5	Latent syphilis	None	None	
6	Tabetic form of dementia paralytica	None	Good	Alkali given throughout course
7	Optic atrophy; tabes	None	Good	Alkali given throughout course
8	Latent syphilis	None	Excellent	Alkali given after 18 injections
9	Cerebral syphilis	None	Increase of weight	Alkali given throughout course
10	Secondary syphilis	Gingivitis	Made mouth painful; refused to continue alkali therapy	
11	Tabes	Pains in joints and muscles; gingivitis	Improved	Marked improvement on addition of fruits to diet
12	Latent syphilis	None	None given	
13	Secondary syphilis; chorioretinitis	None	None given	
14	Latent syphilis	Stomatitis	Excellent	
15	Latent syphilis	Gingivitis	Excellent	
16	Latent syphilis	None	None given	
17	Gumma	None	None given	
18	Syphilitic iritis	None	None given	
19	Primary syphilis	None	None given	
20	Dementia paralytica	None	None given	
21	Gumma	Gingivitis; mercuric dermatitis	Excellent	Skin lesion persisted after disappearance of gingivitis; sodium thiosulphate given
22	Secondary syphilis	Gingivitis	Excellent	
23	Gumma	Stomatitis	Excellent	
24	Gumma	None	.....	In spite of poor dental condition no symptoms developed
25	Dementia paralytica	None	.....	Rapid mental deterioration; alkali given throughout course
26	Syphilitic aortitis	None		
27	Tertiary syphilis	None		
28	Syphilitic nerve deafness	None	Seems to have prevented recurrence of gingivitis	Developed gingivitis with mercuric salicylate, none with colloidal mercuric sulphide
29	Tertiary syphilis	Gingivitis; loss of weight	None given	
30	Secondary syphilis	None	Good	Alkali given and dosage of mercuric sulphide increased
31	Latent syphilis	None	None given	
32	Latent syphilis	None	None given	
33	Latent syphilis	Gingivitis; loss of weight; pains in muscles and joints	Excellent	Alkali and addition of fruits to diet; excellent result
34	Latent syphilis	Pains in muscles and joints; dermal hemorrhages; gingivitis; loss of weight	Excellent	Recovered on scurvy regimen; principally fresh fruits
35	Gumma	Gingivitis	Excellent	
36	Latent syphilis	None	None given	
37	Tabetic form of dementia paralytica	Gingivitis	Excellent	
38	Hemiplegia	Gingivitis	Excellent	
39	Secondary syphilis	Gingivitis	Incomplete	

syphilis except those with primary and/or secondary manifestations had received various amounts of antisyphilitic drugs without satisfactory results.)

An intramuscular injection of 3 cc. of colloidal mercuric sulphide was given twice weekly as a routine in all the foregoing cases. To test the action of the colloidal mercuric sulphide and the alkali when administered concomitantly, some patients were given 4 cc. of mercury twice weekly. They responded equally well to the treatment and showed no untoward action to mercury. In a separate series of more than three hundred intravenous injections in which from 2 to 3 cc. of colloidal mercuric sulphide was given twice weekly the clinical results were equally good and in many cases better than when the drug was given intramuscularly. The number of complications was far less. Although further experimentation is needed before a final opinion can be expressed, I believe the intravenous method to be technically safe and clinically productive of results superior to those cited.

The bluish discolorations are very resistant. In all cases in which they occurred the discolorations are still in evidence after from one to one and one-half years. I am now trying various methods for their removal. In a test tube the brown color can be changed readily either by the addition of an excess of protein or by the combined use of sodium chloride and sodium thiosulphate; but so far no means have been found that will remove the discolorations from the tissues.

COMMENTS AND CONCLUSION

1. The action of colloidal mercuric sulphide is similar to that of metallic mercury.

2. The preparation is powerful and retains all the latent potentialities of metallic mercury.

3. It is painless on administration and causes no palpable infiltrate.

4. It acts very effectively on lesions of the mucous membranes.

5. The slowness of its effects on primary lesions precludes its use in this manifestation.

6. It does not present any preeminent superiority over other antisyphilitic therapy in its ability to change the Wassermann reaction.

7. Its action on the kidneys seems to be first a reduction in excretory function, then irritation and inflammation.

8. It can be highly recommended as a supportive drug, used between courses of neoarsphenamine or neoarsphenamine and bismuth.

9. As a treatment of assault, it should be aided by the supportive effect of arsphenamines and iodides.

10. The co-administration of alkalis prevents complications and aids in their treatment.

11. The drug is not wholly and immediately absorbed.

12. The colloidal suspension is permanent.

13. The dermal discolorations are disfiguring and most resistant to removal.

14. The drug can be given safely both intramuscularly and intravenously. The latter method seems less likely to produce complications.

15. It is effective in other conditions in which mercury is indicated, as lichen planus and verrucae.

16. The lack of toxicity for the blood cells is noteworthy.

PSORIASIS OF THE MUCOUS MEMBRANES

A REPORT OF TWO CASES WITH A REVIEW OF THE LITERATURE

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Psoriasis of the mucous membranes is one of the rarest of dermatologic conditions. Its existence has always been a subject for debate, and to the present day some authorities maintain it does not occur. Darier [1] has only recently denied its existence, and Jadassohn has admitted the possibility of its presence only from reports in the literature.

REVIEW OF THE LITERATURE

In reviewing the literature it is impossible to determine definitely when the writers of the last century were dealing with psoriasis and when with leukoplakia, as the terms were being used synonymously. It was not until 1903 that Oppenheim and Thimm reported the first cases with histologic examination.

Oppenheim's patient [2] presented several plaques, entirely different in appearance from leukoplakia, on the buccal mucosa, the palate and the left palatal vault. The plaques were gray or yellowish white, round or oval and sharply circumscribed. They formed a network with clear spaces in between. The patient, a man, aged 53, had suffered from psoriasis of the skin for twenty years. He was a light smoker, and examination revealed no venereal disease. In discussing the histology Oppenheim emphasized the importance of the presence of parakeratosis, acanthosis and papillomatosis.

Thimm's patient [3] also had buccal lesions associated with psoriasis of the skin. He, too, emphasized the diagnostic importance of acanthosis, papillomatosis and parakeratosis.

During the same year Marcel Sée [4] reported a clinical case without histologic study in a man, aged 23, a heavy smoker. In this patient the tongue, the hard palate and the oral commissures were involved. In the discussion that followed the presentation of this man the members

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From the Department of Dermatology, Montreal General Hospital.

1. Darier, J.: Text-Book of Dermatology, Philadelphia, Lea & Febiger, 1930, p. 104.

2. Oppenheim: Monatsh. f. prakt. Dermat. **32**:489, 1903; abstr., Ann. de dermat. et syph. **6**:379, 1905.

3. Thimm, quoted by Nobl.[6]

4. Sée, Marcel: Ann. de dermat. et syph. **4**:219, 1903.

did not agree concerning the diagnosis, and several thought that the condition was lichen planus.

Although they could not obtain a biopsy, Balzer and Merle [5] felt that their patient, a young woman, presented an instance of psoriasis of the mucous membrane. The right side of the tongue revealed a network of tiny white papules over an area about 1 cm. square. The lesions persisted on and off for one month and then disappeared. The surface epithelium could be scraped off easily, revealing slightly reddened and hypertrophied papillae beneath, but it promptly recurred within from twenty-four to forty-eight hours. There was also extension of the psoriatic process from the lips onto the contiguous mucous membrane.

Nobl [6] quoted several other clinical examples in his monograph, among which were the cases of Wagner and Schutz. None of these authors reported histologic examination of the mucosal lesions.

Within the past decade several other cases have been reported. In Jordan's,[7] that of a woman, aged 27, there was psoriasis of the skin of twenty years' duration. The patient did not smoke and did not have a venereal disease. She presented ring-shaped striae opposite the junction of the teeth and a short distance behind the angle of the mouth. The overlying epithelium could not be scraped off, which is not characteristic of psoriasis of the skin. The histologic examination revealed lengthened and fused rete pegs and parakeratosis. A section from a lesion on the breast showed similar pathologic changes.

In Keller's case,[8] that of a woman, aged 25, there was psoriasis on the body and in the genital region. The patient presented small, grayish-white spots on the buccal mucosa opposite the lower molars. The histologic picture was not that of psoriasis, although histologic examination of the genital lesions showed typical psoriasis.

Schreiner [9] reported a case in a man with typical psoriasis involving the scalp, palms, soles and nails, and presenting plaques on the lips and the hard palate. Histologic examination of the lesions from the mucous membrane and from the skin revealed identical pictures. The buccal and the cutaneous lesions developed together and regressed to the same degree under intensive treatment with arsenic.

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5. Balzer and Merle: Bull. Soc. franç. de dermat. et syph. **18**:78, 1907.

6. Nobl, G.: Psoriasis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 17, book 1, p. 198. This monograph gives a complete bibliography.

7. Jordan, G.: Arch. f. Dermat. u. Syph. **140**:64, 1922; abstr., Ann. de dermat. et syph. **4**:397, 1923.

8. Keller, P.: Dermat. Wchnschr. **75**:917 (Sept. 16) 1922; abstr., Arch. Dermat. & Syph. **7**:664 (May) 1923.

9. Schreiner, K.: Dermat. Wchnschr. **92**:237 (Feb. 14) 1931.

Wesphalen's patient,[10] a man, had suffered from psoriasis of the skin since he was 15 years of age. For the three years before observation the dorsum of the tongue and the buccal mucosa were involved in a whitish, verrucous efflorescence which could not be rubbed or scraped off. The histologic picture was that of psoriasis, i. e., acanthosis, parakeratosis and spongiosis with micro-abscesses in the malpighian layer.

Reil's patients[11] were men, aged 37 and 48, respectively, who presented an efflorescence on the palatal vault and the buccal mucosa, with confirmative histologic changes. The surface epithelium could not be scraped off in either case. Both patients were heavy smokers and drinkers.

Rusch's case[12] also presented involvement of the buccal mucosa with confirmative histologic changes.

Becker and Ritchie[13] recently reported a case of involvement of the oral commissures in a girl, aged 22, associated with plaques on the body and the scalp. On the buccal mucosa the epithelium was thickened and desquamating. The denuded surface was a deeper red than the normal mucosa. The process changed rapidly from day to day. Microscopic study revealed marked intercellular edema and parakeratosis. Cellular infiltration of the mucosa was slight.

Reports illustrating the extension of the psoriatic lesion from the skin to the adjacent mucous membrane appeared in the literature. Pergens and Sack were quoted by Nobl as reporting cases with involvement of the conjunctiva, while Dore,[14] Scheer[15] and Andrews,[16] among others, presented cases with extension of the psoriatic process to the lips. There was no histologic examination in these cases.

In the majority of the cases cited the patient presented lesions in the "cutaneous" region of the cheek, a linear region extending from the oral commissure to the wisdom teeth. Jadassohn called attention to the close association of this region of the mucosa with the skin and to the various lesions such as lichen planus that are found there. The entire literature reveals only three cases of involvement of the tongue associated with psoriasis of the skin, those of Marcel Sée, Balzer and Merle and of Wesphalen. Sée's case was questionable. No biopsy was performed and those who saw the patient thought that the condition

10. Wesphalen, H.: Dermat. Ztschr. **54**:402 (Nov.) 1928.

11. Reil, H.: Dermat. Ztschr. **32**:215, 1921.

12. Rusch: Wien. dermat. Gesellsch. **26**:3, 1925; quoted by Nobl.[6]

13. Becker, S. W., and Ritchie, E. B.: Arch. Dermat. & Syph. **22**:745 (Oct.) 1930.

14. Dore: Proc. Roy. Soc. Med. **17**:84, 1924.

15. Scheer, M.: Arch. Dermat. & Syph. **9**:594 (May) 1924.

16. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930.

might be lichen planus. Doubt could also be thrown on the case presented by Balzer and Merle. The patient had gonorrhea and no histologic examination was made. Hallopeau, who discussed the case, suggested syphilis as an etiologic factor. Wesphalen's patient appears to be the only one whose psoriasis was proved. In his case histologic examination of the mucosal lesion showed the same changes as those in a lesion from the skin.

As a rule, the mucous membranes of patients with psoriasis were not examined. It is possible that psoriasis of the mucosa has been overlooked. Lissauer [17] found involvement of the buccal mucosa in ten of his series of fifty patients. He considered the condition leukoplakia and attributed it in every case to smoking. In discussing Marcel Sée's case,[4] Baudouin stated that he had seen only two undoubted examples of leukoplakia in a series of thousands at the Hôpital Saint-Louis. Scheer and Schreiner also stated that a routine examination of many patients with psoriasis seen over a period of years showed no lesions of the mucosa which even remotely resembled psoriasis except in the cases reported. With this in view, I examined the buccal mucosa of one hundred consecutive patients with psoriasis. Lesions of the buccal mucosa were noted in three patients. Clinical and histologic examinations revealed that in one of these patients, a man, aged 40, the condition was leukoplakia. The condition in the other two patients was diagnosed as psoriasis.

REPORT OF CASES

Case 1.—*History.*—W. G., a laborer, aged 24, presented himself at the dermatologic outpatient department of the Montreal General Hospital on May 30, 1932. He complained of a cutaneous eruption which he had first noticed three years before. The attack which brought him to the hospital was the third and was of three months' duration. The eruption usually appeared during the summer and cleared up spontaneously with the approach of cold weather. With each attack, "his tongue became coated and red, and felt peculiar." He observed that it improved coincidentally with the cutaneous manifestations, but never entirely returned to its normal state. He had never received medical attention.

His past history was irrelevant. He smoked only cigarets and those in moderation. He said that he had not had a venereal disease.

Cutaneous Lesions.—He presented two large plaques, one on the left side of the body and one on the left leg. Each was about 3 inches (7.6 cm.) in diameter. The lesions were sharply outlined, dull red and covered with a thick scale. The scales were silvery-white and micaceous, and they became more apparent on scraping. Gentle grattage revealed characteristic minute bleeding points.

The tongue was involved in a curious and bizarre manner. It was scrotal in type, the grooves being more pronounced because the organ was beefy and red, and larger than normal. The tongue was involved from the circumvallate papillae posteriorly to the tip anteriorly, the sides and the under-surface also being affected. The lesions varied in size from minute split pea-sized papules to those fully

17. Lissauer, quoted by Balzer and Merle.[5]

Fig. 1 (case 1).—View of the under-surface of the tip of the tongue.

Fig. 2 (case 1).—Low power photomicrograph showing changes in the rete malpighii.

one-half inch (1.27 cm.) in diameter. They were round and sharply demarcated, and showed little tendency to become fused. They not only were present on the mucosa between the sulci but extended deeply into the sulci as well. The papules were covered with a superficial layer of grayish-white epithelium which could be scraped off fairly easily. A moderately reddened surface with prominent papillae was then apparent. The eruption on the under-surface of the tip of the tongue varied somewhat from the other eruption on top. On each side of the midline was a sharply circumscribed, large oval plaque extending from the tip to the attachment posteriorly. The plaques were reddened and denuded of surface epithelium. There was a small, grayish-white patch on the buccal mucosa opposite the right upper molar. The rest of the mouth was clear.

The remainder of the body was unaffected.

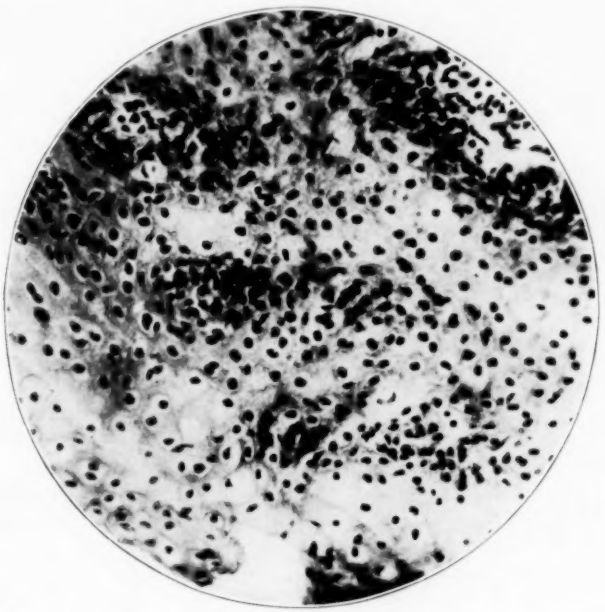

Fig. 3 (case 1).—High power photomicrograph showing the infiltrate in the rete malpighii and the presence of micro-abscesses.

Routine laboratory examination revealed a normal blood chemistry, a basal metabolic rate of —15 and on three occasions a negative Wassermann test of the blood. Laryngologic consultation reported no extension of the process downward. The tonsils were infected, and roentgen examination showed slight cloudiness in the right antrum.

A potassium hydroxide preparation of scrapings from the tongue revealed no mycelia or yeast cells. Culture of the scrapings revealed a nonpathogenic mold.

A biopsy was made on a plaque on the under-surface of the tip of the tongue. The sections were prepared in the usual manner and stained with hematoxylin and eosin. The stratum corneum was for the most part absent. Where it still persisted, there was marked parakeratosis. The stratum granulosum was thinned, and was for the most part absent. The suprapapillary portion of the malpighian

layer was of normal thickness, but the pegs were elongated; they showed little change in breadth. The blood vessels in the papillary portion of the corium were dilated, with a marked infiltration of round cells about them. In some parts of the sections there were numerous polymorphonuclear neutrophils as well. Numerous round cells and occasional polymorphonuclear cells could be seen in the epidermis, as well as occasional minute vesicles and micro-abscesses containing round cells and polymorphonuclear neutrophils. No plasma or mast cells were apparent. The collagen fibers presented slight edema, but were otherwise unchanged.

No biopsy was performed on the lesions of the body, because before the lingual eruption was noted the patient had been treated with an ointment containing salicylic acid, chrysarobin, oil of cade, soft soap and wool fat.

Fig. 4 (case 2).—Low power photomicrograph of a section from the buccal mucosa.

Following treatment with solution of potassium arsenite, U. S. P., by mouth and the aforementioned ointment locally, striking improvement was apparent. In six weeks the skin and the mucous membranes were entirely normal. The patient reported again for observation three months later. Although the skin was clear, there was beginning recurrence of the lingual lesions, on both the upper and the lower surfaces. Continued administration of arsenic again resulted in cure, but when the drug was discontinued, the lingual involvement reappeared.

Case 2.—*History.*—I. M., a girl, aged 13, presented herself at the dermatologic outpatient department of the Montreal General Hospital on July 5, 1926. She complained of a cutaneous eruption which was first noticed three years before. The skin cleared up with local administrations of chrysarobin and subcutaneous injections of sodium cacodylate. The patient was next observed in

April, 1932, with a marked attack of psoriasis and a history of having had recurrences during the winter and remissions during the summer. The skin remained clear during the summer. In November, 1932, the patient returned with a severe recurrence of the psoriasis. The buccal involvement was noted at this time. Unfortunately, the mucosae had not been examined on the previous visits to the clinic.

The patient's past history was irrelevant. She smoked three or four cigarets daily. She said that she had never had a venereal disease.

The cutaneous lesions were large, gyrate patches, typical of psoriasis, involving almost the entire trunk and extremities. The face was clear, but the scalp was extensively affected.

There was extensive involvement of the buccal mucosa from the anterior commissures to the anterior fauces posteriorly. There was a fairly coarse interlacing network of grayish-white striae enclosing unaffected mucous membrane. The papules were only slightly raised above the unaffected parts, and the epithelium could be scraped off only with difficulty. The tongue and the palate were unaffected.

Routine physical and laboratory examinations revealed nothing abnormal. The Wassermann test of the blood was negative. Scrapings from the mouth revealed nothing of significance.

Histologic examination was made of lesions from the body and from the buccal mucosa. The sections from the body revealed a picture which was characteristic of psoriasis. There were parakeratosis and almost complete absence of the granular layer. Acanthosis was present with papillomatosis and clubbing of the pegs. The corium revealed a mild degree of vascular dilatation and infiltration with round cells.

The sections from the mouth did not reveal a characteristic picture. There were marked parakeratosis and absence of the granular layer. The malpighian layer was markedly acanthotic, and the malpighian pegs were somewhat elongated. The suprapapillary portions of the malpighian layer were broadened, and there was no clubbing of the pegs. Although a few wandering lymphocytes could be seen, there were no micro-abscesses present. A moderate degree of vascular dilatation and infiltration with round cells was present in the corium.

Under treatment with gold and sodium thiosulphate intravenously the eruption on the trunk cleared up almost entirely, and the buccal lesions concomitantly showed considerable improvement. At present there are a few guttate patches on the extremities, but the trunk is clear. The eruption in the mouth shows faint traces of the original eruption. No local therapy was used on the skin or in the mouth.

COMMENT

The features of the first case which were suggestive of the psoriatic nature of the lesions on the surface of the tongue were: the clinical course, closely paralleling that of the eruption on the body; the absence of irritating factors, such as syphilis and tobacco, which might account for leukoplakia; the desquamation of the epithelium with prompt recurrence, and finally, the changes seen in the histologic section. While the sections were not entirely typical, their chief features—acanthosis, papillomatosis and parakeratosis—made the condition compatible with psoriasis, especially when one took into consideration the maceration which affects a lesion on the under-surface of the tongue.[17] The diseases

17. Weidman, F. E.: Personal communication.

which one might consider—leukoplakia, geographic tongue, lichen planus or an infection due to yeast—could be ruled out without difficulty because of the clinical course of the eruption and because of the laboratory findings.

In the second patient the diagnosis of psoriasis was made with a certain degree of reservation. The overlying epithelium in the second case, unlike that of the first case, could be scraped off only with difficulty, and the underlying bleeding was not characteristic. Moreover, the histologic sections from the mouth were not characteristic of psoriasis, and were not similar to those from the body. From the sections alone a diagnosis of leukoplakia could be made. Against a diagnosis of leukoplakia were the sex and the age of the patient and the absence of syphilis, excessive smoking or other irritative factors. The diagnosis of buccal psoriasis was made entirely from the clinical course of the eruption. The coincidental appearance of the lesions on the mucosa and on the body, their reaction to treatment with a gold compound with no local therapy and, finally, their subsidence would appear to substantiate the diagnosis of psoriasis.

VITILIGO

A CLINICAL AND HISTOLOGIC STUDY, WITH A CONSIDERATION OF PINTA

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CHICAGO

Since the advent of modern study of pigment, little has been done toward the solution of the problem of vitiligo. Bloch [1] noted absence of the dioxyphenylalanine reaction in the depigmented region. Miescher [2] utilized a patch of vitiligo in some of his studies of chromatophores and found that chromatophores in the depigmented areas take up melanin injected intradermally. McCarthy [3] stated that the histologic change consists of disappearance of the chromatophores (melanoblasts [S.W.B.]) from the cells of the lower portion of the epithelium. Gans [4] noted partial or complete depigmentation of the patches of vitiligo with hyperpigmentation of the border. He stated that inflammatory and atrophic changes have been observed, along with nerve changes of the atrophic type. He appropriately called attention to the difficulty in interpretation of cutaneous nerve sections. Nadel [5] studied the pigment which had appeared in treated vitiliginous patches and determined it to be melanin.

ETIOLOGY

Strandberg [6] called attention to the symmetrical appearance of the lesions, their development following shock, their association with a neurogenic constitution and other characteristics. The condition has been found in association with hypothyroidism and hyperthyroidism,

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From the Section of Dermatology of the Department of Medicine, the University of Chicago. Read in part at the Scientific Session of the Section of Dermatology, Nov. 6, 1931.

1. Bloch, B.: Zur Pathogenese der Vitiligo, Arch. f. Dermat. u. Syph. **124**: 207, 1917.

2. Miescher, G.: Die Chromatophoren in der Haut des Menschen, das Wessen und die Herkunft ihres Pigmentes, Arch. f. Dermat. u. Syph. **139**:313, 1922.

3. McCarthy, Lee: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931.

4. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1.

5. Nadel: Demonstration of Histologic Preparations from a Treated Vitiliginous Patient, Zentralbl. f. Haut.- u. Geschlechtskr. **33**:149, 1930.

6. Strandberg, J.: Haut und innere Sekretion, in Jadassohn, J.: Handbuch für Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 3.

dermographism, lichen simplex chronicus and alopecia areata. I have noted it in connection with neurodermatitis and with neurotic excoriations. The basal metabolic rate is said to be abnormally high or low. Strandberg cited Levy, Franckel and Juster as having observed the same capillary constriction as is found in alopecia areata and in the finger-tips in certain conditions. The capillaries were difficult to find in the depigmented zone. Strandberg stated that Flarer studied twenty cases of vitiligo. In fifteen he found vascular lability with a strong reaction of the vasoconstrictors to epinephrine and of the vasodilators to pilocarpine. Flarer is said to have stated that most probably a trophoneurotic disturbance is present in the field of the vegetative nervous system. Takigawa [7] concluded that vitiligo has a connection with the glands of internal secretion or the vegetative nervous system. Ninety-five per cent of his patients were sympathicotonic, and 100 per cent were vagotonic. In my study of patients with neurocirculatory instability,[8] I noted that all patients with vitiligo exhibited various signs and symptoms present in that condition. The basal metabolic rates in my patients were low, and the blood pressures were low.

TREATMENT

All methods of therapy have been unsatisfactory with the exception of ultraviolet irradiation, with or without photosensitizing substances administered intravenously (acriflavine hydrochloride) or orally (acriflavine hydrochloride) or applied directly to the patches (oil of bergamot or perfumed spirit). This has resulted in benefit in some cases, but has been without result in most instances. Lindsay [9] injected gold and sodium thiosulphate intravenously and reported subsequent improvement in some cases. This treatment has been practically without result in a few cases in the University of Chicago clinics. Attempts at organotherapy have been unproductive.

RESEARCH

Two patients with vitiligo were treated by frequent exposure to ultraviolet radiation, and sections were removed from the border of the eruption at frequent intervals. My purpose was primarily to study melanoblasts and to attempt to locate them in nonpigmented tissue, as well as to observe their behavior following exposure to ultraviolet radia-

7. Takigawa, K.: Studien über Vitiligo vulgaris, Jap. J. Dermat. & Urol. **30**: 105, 1930.

8. Becker, S. W.: Dermatoses Associated with Neurocirculatory Instability, Arch. Dermat. & Syph. **25**:655 (April) 1932.

9. Lindsay, H. C. L.: Treatment of Leukoderma with Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **20**:22 (July) 1929.

tion both in pigmented and in nonpigmented regions. It is well known that in normally pigmented regions they increase in size after irradiation and assume a dendritic form (Peck[10]). Whether the change in size and form depends on pigmentary function or whether the two functions are independent has not been studied previously.

CASE 1.—*History.*—A nurse, aged 37, for many years had had large patches of vitiligo on the arms, hands, legs and feet. A section was removed for biopsy on Oct. 25, 1930, and daily ultraviolet therapy was instituted. Later the treatments were given every other day. Additional sections were removed on November 8 and 22 and December 6. The pigmented region became hyperpigmented, but no pigment appeared in the depigmented region.

Microscopic Study.—The transition from the pigmented to the depigmented region was rather abrupt. Pigmentation was normal on one side of the border and absent on the other side. After one week's exposure to ultraviolet radiation dendritic cells were numerous in the pigmented region but were not seen in the depigmented region. In the depigmented region mitotic figures were present in greater numbers than normally, and the epidermodermal junction was regular, with no cellular infiltration. In the pigmented region, on the other hand, the epidermodermal junction was irregular, there was mild cellular infiltration, and the melanoblasts were larger and more dendritic than normal. In sections of tissue removed later this was not so marked, but the palisade basal cells became more and more pigmented. No pigment was found in the depigmented region at any time. This corresponded to absence of pigment in the vitiliginous patches after irradiation.

CASE 2.[11]—*History.*—A housewife, aged 45, had neurodermatitis of the eczematoid, exudative type. For many years she had had vitiligo on the body and the extremities (figs. 1, *A*). A section was removed from the border on Dec. 23, 1930, and daily exposure to ultraviolet radiation was instituted. Additional sections were removed on Jan. 7 and 28, 1931, February 19 and March 25. The patient was again seen on Nov. 5, 1931; at that time there had been some extension of the pigmented region adjacent to the border (fig. 1, *B*), although the hyperpigmentation had subsided.

Microscopic Study.—The demarcation between the pigmented and the nonpigmented portion was not so definite as in case 1, and there was a small amount of pigment in the depigmented portion in the form of dendritic cells and a few pigment granules in adjacent basal cells. After ultraviolet irradiation for one week the dendritic cells were more prominent (fig. 2). In the depigmented portions the epidermis was regular and did not contain large melanoblasts (fig. 3, *A*). There were, however, small cells in the innermost portion of the basal layer which corresponded to the "cellules claires" of Masson,[12] which he considered as precursors of melanoblasts. They had small nuclei with a small amount of granular protoplasm, somewhat more basophilic than that of the palisade basal cells. In the pigmented portion the epidermodermal junction was somewhat irregular, and some cellular infiltrate was seen (fig. 3, *B*). Instead of the small "cellules claires" seen

10. Peck, S. M.: Pigment (Melanin) Studies of the Human Skin After Application of Thorium X, Arch. Dermat. & Syph. **21**:916 (June) 1930.

11. This case was presented at the Scientific Session of the Section of Dermatology of the Department of Medicine, of the University of Chicago, Nov. 6, 1931.

12. Masson, P.: Les naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**:417 and 657, 1926.

in the depigmented portion, cells having larger nuclei and more extensive protoplasmic bodies were seen. The protoplasm was granular and somewhat basophilic. In silver preparations these were seen to be the pigmented dendritic cells described during pigmentary activity.

PIGMENTARY AND DEPIGMENTARY PROCESSES IN PINTA

Through the courtesy of Dr. Howard Fox I studied sections from several cases of pinta (mal del pinto, carate). (He was the first to

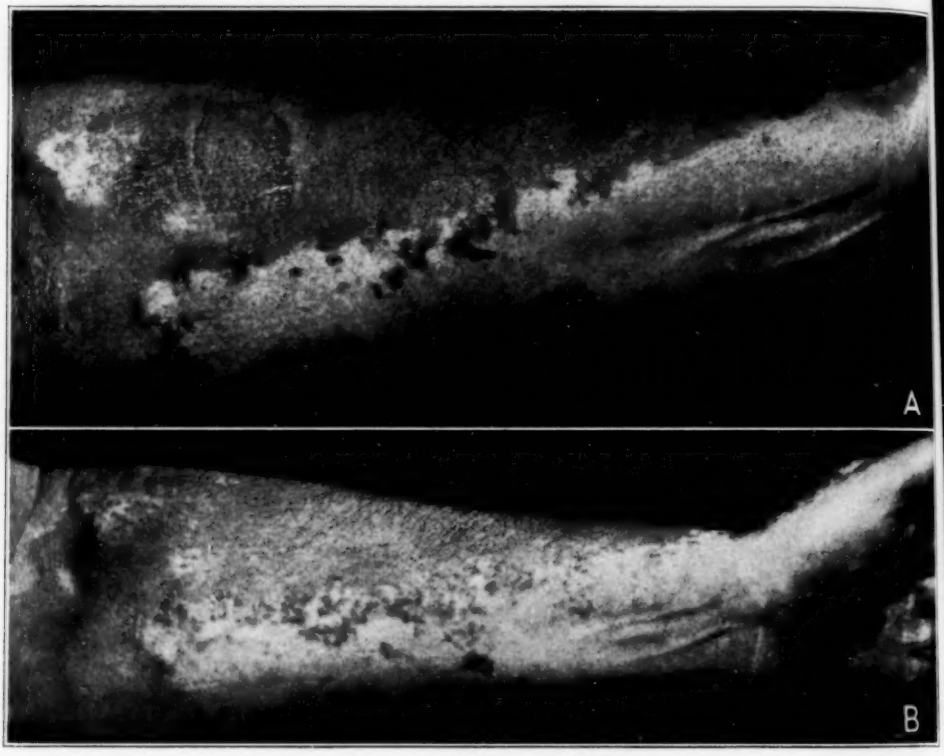

Fig. 1 (case 2).—*A*, a patch of vitiligo on the flexor surface of the forearm after three and one-half months of ultraviolet radiation. *B*, the same patch seven months later. The hyperpigmentation has decreased somewhat, and small islands of newly pigmented epidermis are seen, especially near the border.

study thoroughly both pinta and carate and establish them as the same disease.[13]) The fact that this condition eventuates in vitiligo-like depigmentation suggested that additional information might be derived from

13. Fox, H.: Carate (Pinta) as Observed in Colombia, South America, Arch. Dermat. & Syph. **18**:673 (Nov.) 1928; Mal del Pinto as Observed in Mexico; Its Relation to Carate, Proc. Eighth Internat. Cong. Dermat. & Syph., Copenhagen, 1930, p. 510.

the study of these sections. From the clinical standpoint the condition may be divided into four stages: first, a very early stage in which the normal pigmentation can still be evaluated; second, an inflammatory stage, corresponding clinically to the erythematous stage; third, a stage of marked dermal pigmentation, which is clinically the blue stage, and fourth, a stage of depigmentation, clinically similar to vitiligo.

The sections were stained by three methods: first, hemalum-erythrosine and safranine for general study; second, silver nitrate, counterstained with pyronine-methyl green, for the detailed study of melanin, and third, Masson's trichrome (iron hematoxylin, acid fuchsin, ponceau de xylidine, aniline blue). The last-mentioned method, or a similar one, is necessary for cytologic study, and a study of this kind cannot be made with ordinary hematoxylin and eosin or similar stains.

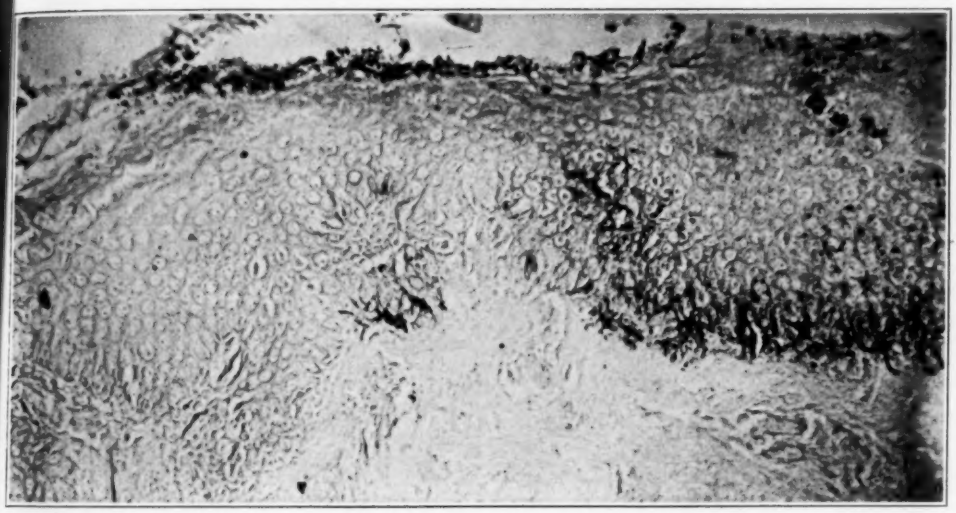

Fig. 2 (case 2).—A section from the border of a patch of vitiligo one week following ultraviolet radiation. Pigmentary activity is evidenced by dendritic cells. Two cells are plainly seen toward the depigmented portion. Oil-immersion, silver nitrate preparation; pyronin-methyl green counterstain.

The first stage (fig. 4, A) showed a normal darkly pigmented skin (this condition is found largely in dark races) with slight dermal inflammation. Pigmentation was so marked that recognition of melanoblasts was difficult in silver nitrate preparations, but they could be seen to be normal in trichrome-stained sections. The second, or inflammatory, stage (fig. 4, *B*) showed marked acanthosis with only slight pigmentation. Melanoblasts were prominent as elongated cells at the epidermo-dermal junction. The dermis showed vascular dilatation, edema and round cell infiltration. The third stage (fig. 5, *A*) showed the most marked dermal pigmentation that I have ever seen, with many tiers of chromatophores in the superficial dermis. The epidermis had returned to its normal thickness and contained more pigment than in the inflammatory stage. Melanoblasts were more prominent than normally. The fourth stage (fig. 5, *B*) showed in places complete depigmentation

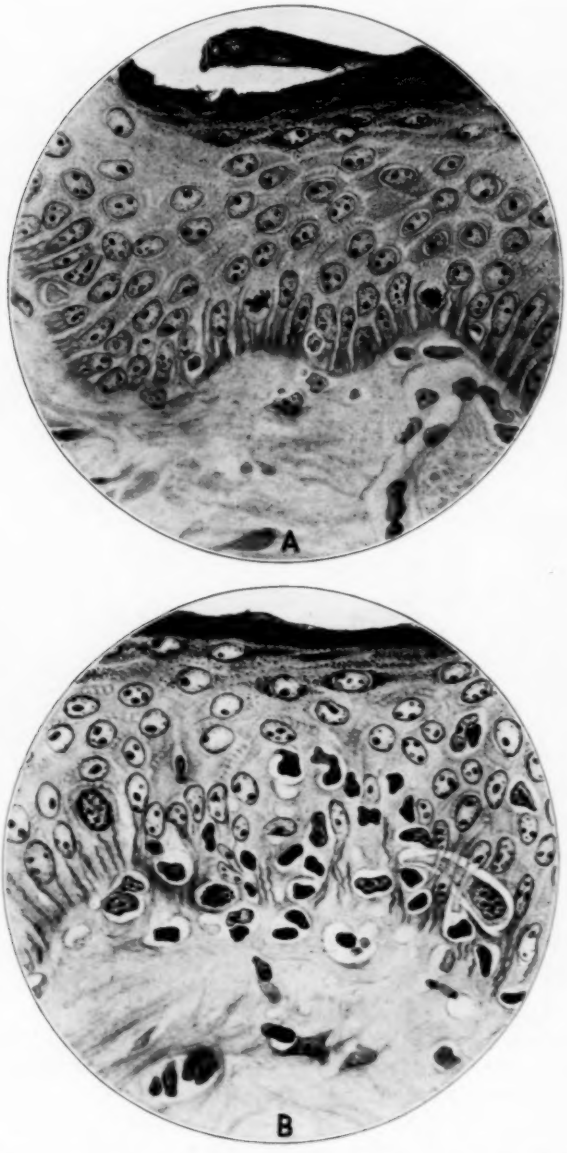

Fig. 3 (case 2).—*A*, a vitiliginous patch after one week of ultraviolet radiation. The epidermodermal junction is regular. Cellules claires of Masson are present. *B*, The pigmented border after one week of radiation. The epidermodermal junction is irregular, and one large melanoblast is plainly visible. Many wandering cells are present. Oil-immersion preparations; Masson trichrome stain.

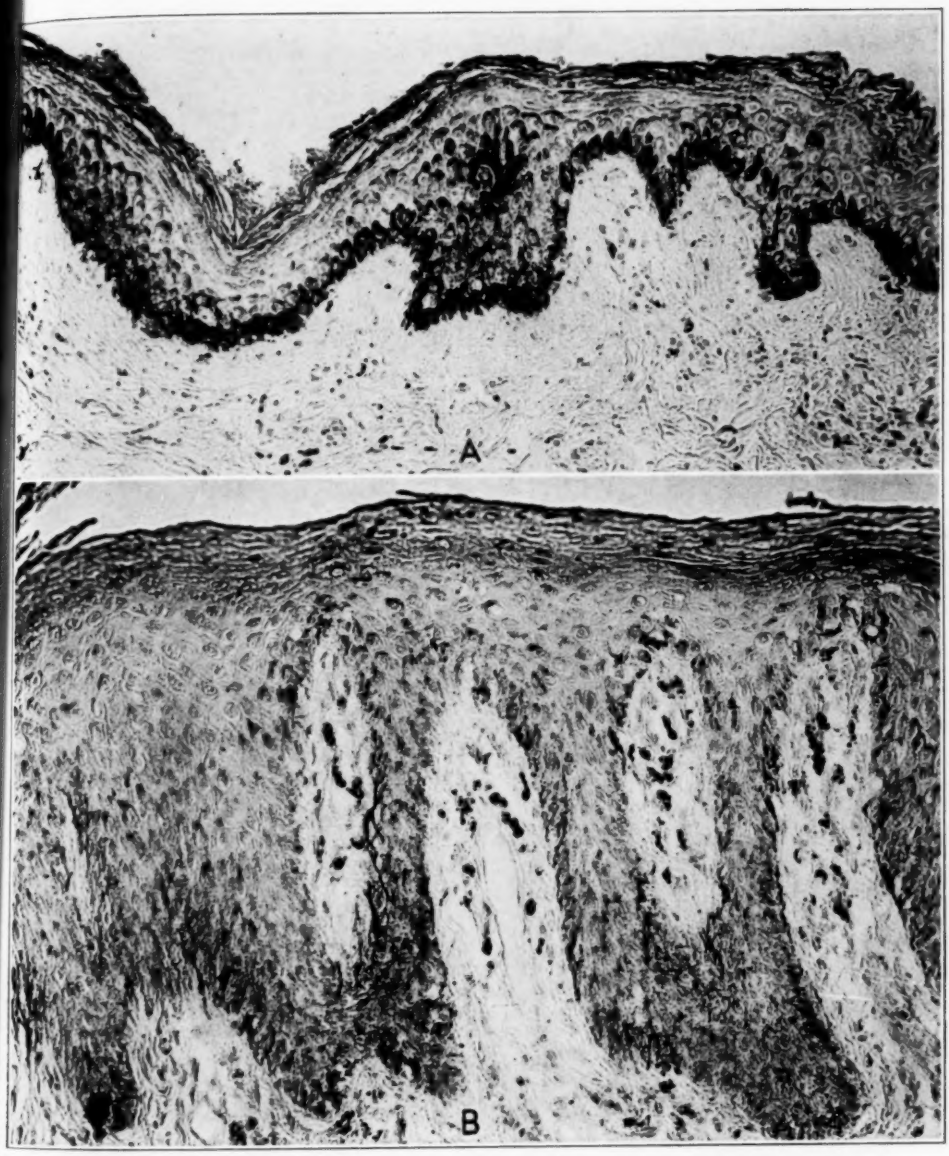

Fig. 4.—*A*, pinta. The epidermis is deeply pigmented, with slight inflammatory changes in the dermis. *B*, marked acanthosis. Pigmentary activity is present in the form of dendritic melanoblasts. There is a moderate number of chromatophores.

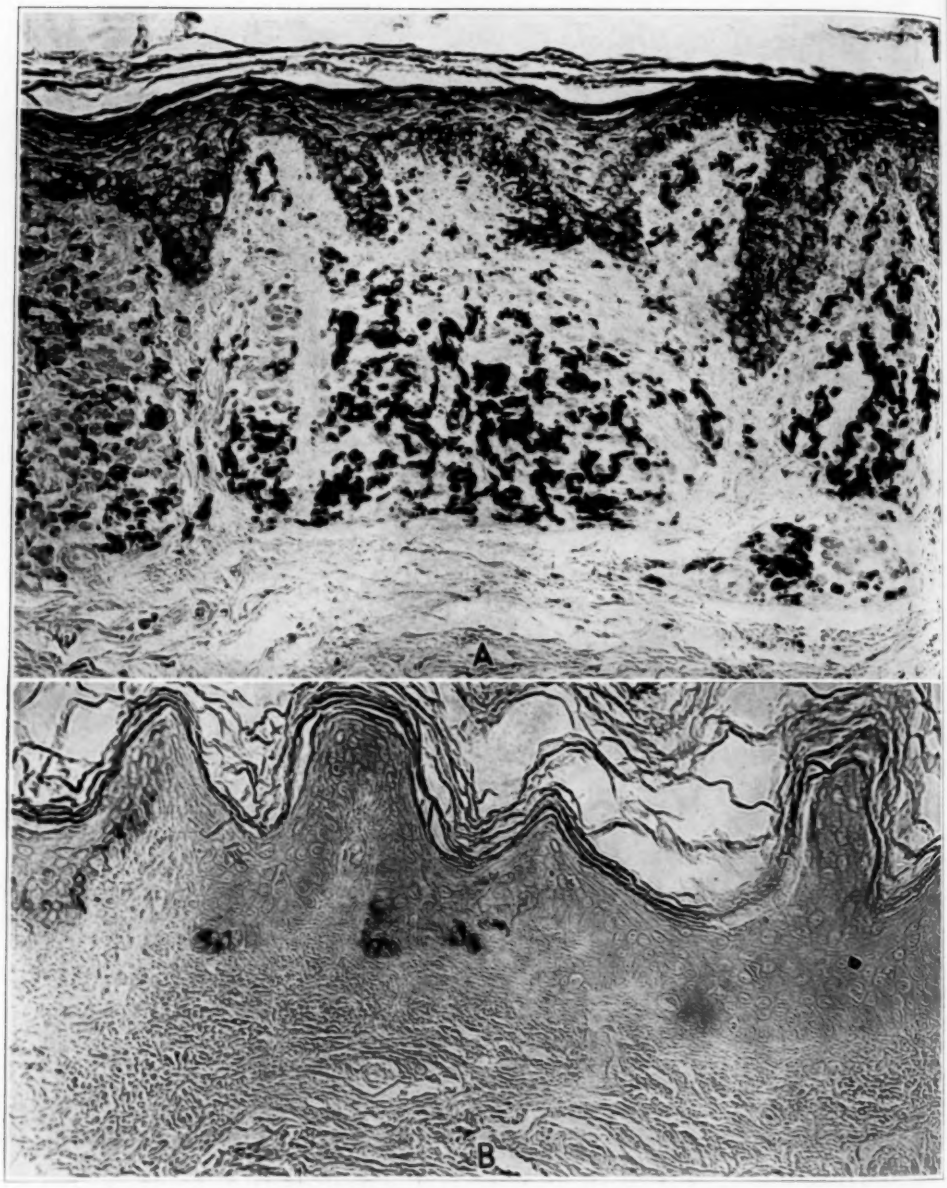

Fig. 5.—*A*, enormous deposition of melanin in the chromatophores. The epidermis is hyperpigmented and of about normal thickness. *B*, border of the depigmented area, showing gradual transition from the pigmented to the nonpigmented region. Silver nitrate preparations; counterstained with pyronin-methyl green.

of the epidermis and dermis, with gradual appearance of pigment toward the border of the depigmented lesion. Cells of the type which Masson called cellules claires were almost entirely absent, in contrast to the depigmented plaques of vitiligo where they were present as small cells.

COMMENT

1. It was difficult to orient the material so that sections were always cut at a right angle to the border between the pigmented and the depigmented portion. This increased the difficulty in interpreting the sections.

2. A cellular reaction was noted in the region of active pigment production, although there was none in the depigmented portion. This consisted of irregularity of the junction between the epidermis and the dermis, the presence of dendritic melanoblasts and a definite infiltrate in this region with some of the infiltrating cells extending high up into the epidermis. They were evidently wandering cells. This type of reaction in the pigment-producing tissue was not merely the result of the ultraviolet radiation since the nonpigmented portion was also exposed to the ultraviolet rays and showed several mitotic figures as evidence of reaction. The type of reaction found in the pigment-producing tissue was also found in sections from lentigo of the palm in which there was no possibility of stimulation by ultraviolet rays. This particular reaction associated with pigment production has never been mentioned in the literature to my knowledge.

3. Distinctive cells (cellules claires of Masson [12]) were seen in depigmented regions. These are small cells located in the basal portion of the epidermis between the palisade basal cells. They are shown plainly in figure 3. Masson expressed the belief that these have some connection with the nervous system, and that they are the cells which form dendritic melanoblasts under certain definite stimuli. They have small nuclei and a granular protoplasm tending to be basophilic. They are often surrounded by a vacuole or a pseudovacuole. These cells do not have the acidophilic fibrillae that are possessed by palisade basal cells.

4. In pigmented regions larger cells, often arranged with their long axes parallel to the epidermodermal junction, containing basophilic protoplasm and pigment granules, were seen. These were dendritic melanoblasts. It was difficult in my sections to demonstrate any transition from the small cells in the depigmented region to the large cells in the pigmented region, although they had the same general characteristics and varied considerably in size in the two regions.

5. It is impossible to state whether these cells were more numerous in the pigmented than in the nonpigmented regions. They were more branched and larger in the pigmented regions and consequently seemed more prominent. There was no evidence that these cells were becoming more numerous under the stimulus of ultraviolet therapy.

6. No connections between these cells and structures in the dermis could be seen. Masson believed that he had seen such connections. One of the greatest deficiencies in dermatologic histology is the inability to demonstrate satisfactorily nonmedullated nerve fibers in the skin.

7. No increase in size was noted in these cells in the nonpigmented region, and they did not become pigmented. It seems, therefore, that the increase in size and the formation of pigment are associated functions.

8. The pigmentary process in pinta originates in an inflammatory reaction followed by increased pigment activity, as shown by the formation of dendritic cells, and the most marked retention of pigment in chromatophores that is found in any pigmentary dermatosis with the possible exception of melanoma. This deposition of pigment in chromatophores extends so deeply that a bluish color is given to the skin, as is found in blue nevus, rather than simply a slate gray color as is found in conditions associated with slight or moderate chromatophore pigmentation. Depigmentation in pinta is associated with the disappearance of melanoblasts and even of the small cells (cellules claires of Masson). This is in contrast to what is found in vitiligo and may be a factor in the complete resistance of the depigmented patches to therapy. In vitiligo it is not uncommon to have partial or complete restoration of pigmentary function, but in pinta this is said not to occur. Sections from the center of a depigmented patch of vitiligo may show absence of the "cellules claires." This region was not examined.

SUMMARY

Two cases of vitiligo were studied by means of ultraviolet radiation and repeated examination of microscopic sections at the border. Pigmentary activity was noted in the pigmented region, and in one case there were signs of such activity along the border of the depigmented region. Clinical return of a small amount of pigment followed ultraviolet radiation in this case, but not in the other, in which no pigment was visible microscopically. Cellules claire of Masson were found in the depigmented regions. An inflammatory reaction characterized by irregularity of the epidermodermal junction and cellular infiltration of the epidermis accompanied pigmentary activity, as seen in the formation of dendritic melanoblasts. This inflammatory reaction has also been found in lentigo of the palm and has not been mentioned previously in the literature. Sections from the various stages of pinta showed first an inflammatory reaction with marked acanthosis and pigmentary activity. This was followed by the most marked chromatophore pigmentation that has been seen in any pigmentary dermatosis, with the possible exception

of melanoma. The pigment was gradually absorbed, and the patch became completely depigmented. This was associated with a disappearance of all cells which might be construed as cellules claires of Masson or as melanoblasts. This complete disappearance may be the reason for the relatively greater resistance to therapy found in the vitiligo-like patches of pinta as compared with vitiligo.

VINCENT'S DISEASE ASSOCIATED WITH AN ERYTHEMA MULTIFORME-LIKE ERUPTION

REPORT OF A CASE

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Lesions of the skin associated with Vincent's disease are of rare occurrence in dermatologic practice and reports of this association are rare in medical literature. Pusey, Sutton and others have hardly mentioned such an occurrence in their textbooks. Andrews [1] referred to two cases of Vincent's fusospirillary dermatitis reported by Greenbaum,[2] one of the external auditory canal and the other of the hands and vulva. Other than this, mention of an eruption on the hands associated with Vincent's disease is practically missing from the literature. Having recently treated a patient in whom an erythema multiforme-like eruption was present on both hands as a complication of a severe Vincent's infection of the mouth, I believe that the case might well be added to the list of reported cases.

The lesions were symmetrically distributed, as is shown in the figure, and showed characteristics which more or less suggested erythema multiforme. Marked itching was present, as well as severe constitutional symptoms. Although it is realized that typical erythema multiforme may disappear spontaneously, it is interesting to note that in this case the lesions of the mouth and skin cleared up promptly following intravenous administration of arsphenamine.

REPORT OF CASE

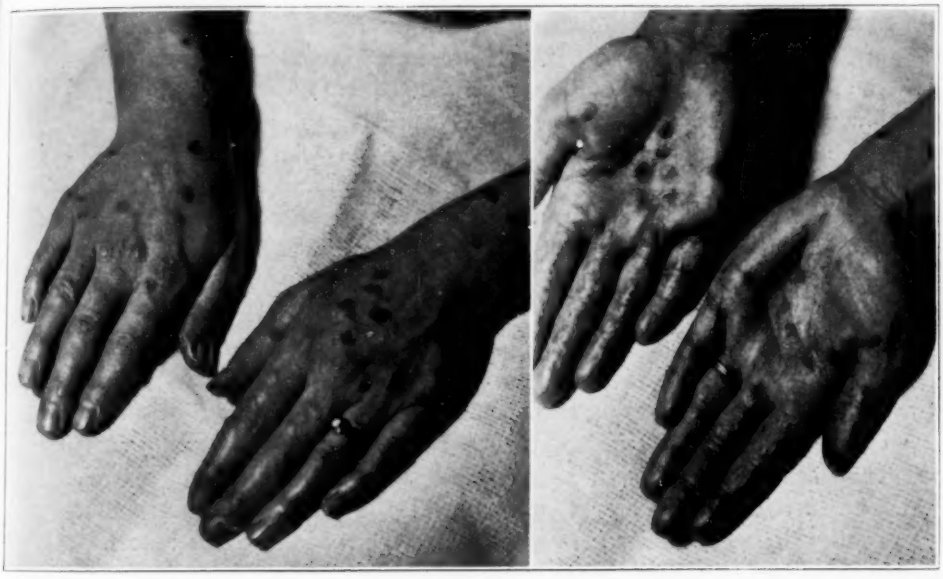
Mrs. C. M., aged 25, was brought to my office on the evening of March 17, 1933, by her physician, Dr. C. C. Williamson of Gorham, N. Y. She was suffering from a terrific stomatitis, with visible salivation, and had a strong fetid odor of the breath. Both hands were wrapped in cloths. Owing to extreme pain in the mouth produced by her attempts to eat, she had been unable to take nourishment in the form of food or drink, except very greasy broth, for five days. Even milk was intolerable. She could open her mouth for oral examination only with difficulty. A tentative diagnosis of Vincent's angina was made, and the smears which were taken were all positive for the fusiform spirillum of Vincent.

The skin of her hands presented a peculiar picture, which might be described as that of a discrete papular eruption, most of the lesions showing crater forma-

1. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930.

2. Greenbaum, S. S.: Fusospirillary Dermatitis, Arch. Dermat. & Syph. **15:** 678 (June) 1927.

tion, with a slight crusting of the depressed centers. There was a close resemblance to the picture usually presented by erythema multiforme. Considerable erythema was present about the base of each lesion. The only subjective symptoms were itching and burning. The palmar surface of the fingers showed a peculiar linear type of encrusted vesicular dermatitis, from which oozed considerable deep yellowish serum with the same characteristic fetid odor. The photographs were taken by the light of a quartz lamp, as it was evening and the patient intended to return home after the treatment. Arsphenamine in a dose of 0.5 Gm. was given intravenously on this visit. The next noon the patient's physician called, stating that he had just seen the patient and that she was able to enjoy with relish some liquid nourishment during the morning. The following day she ate food. The



Photograph of the dorsal and palmar surfaces of the hands. Note the discrete arrangement of the lesions, some of which have small vesicles in their depressed centers. Some clearly show the crater-like formation. In addition, the palmar surfaces show a linear type of encrusted vesicular dermatitis on the fingers, which is best illustrated on the third and fourth fingers of the right hand.

condition of the hands improved with equal rapidity. Five days later another 0.5 Gm. of arsphenamine was administered, at which time the lesions of the mouth had nearly all cleared up and the lesions on the hands were undergoing desquamation. Oozing from the vesicles on the fingers had stopped. A week later the eruption had subsided except for a slight trace of desquamation at the site of the worst lesions. Complete recovery followed. No local treatment was used purposely on the lesions of the skin, and no oral treatment was necessary. The Wassermann reaction of the blood was negative.

407 South Main Street.

CALCIFICATION OF THE SKIN AND SUBCUTANEOUS TISSUES (CALCINOSIS)

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S. BARRE PAUL, M.D.

GLANVILLE Y. RUSK, M.D.

AND

EDWARD A. LEVIN, M.D.

SAN FRANCISCO

Abnormal deposits of calcium salts in the various tissues of the body are a frequent occurrence. These are found commonly in arteriosclerotic patches, in caseous tuberculous nodules and in chronic lesions following a pyogenic infection such as calcification of the pleura; also secondary to fat necrosis, in thrombosis of the veins and arteries, following trauma and occasionally in certain benign and malignant tumors. Calcification occurs rarely in the skin and subcutaneous tissues.

The term calcinosis is used by Durham [1] to indicate the abnormal presence of calcium in any of the tissues of the body. Most authors, however, limit its meaning to those instances in which the pathologic calcification is found in the skin and subcutaneous tissues. Two forms are recognized. One is the result of a disturbance in calcium metabolism; the other is the result of metastasis of calcium salts from normal depots of calcium in the body. The latter form occurs as a result of bone destruction, as seen in osteomalacia, osteomyelitis and leukemia. The mechanism of these changes is little understood. A case illustrating the metabolic type of calcinosis is the subject of this report.

HISTORICAL REVIEW

In 1878, Weber recorded the earliest case of calcinosis. Several of the early case reports appeared in the French literature under the term "Profichet's syndrome." Hunter [2] observed two patients in 1913; he stated that he could find reports of only two other cases in the English literature, and that he was able to discover only eight cases in the continental literature. In 1911, Thibierge and Weissenbach [3]

From the Department of Dermatology and Syphilology and the Department of Pathology of the Mount Zion Hospital.

1. Durham, R. H.: Scleroderma and Calcinosis, Arch. Int. Med. **42**:267 (Oct.) 1928.

2. Hunter, W. K.: Scleroderma with Subcutaneous Calcareous Deposits, Glasgow M. J. **79**:241, 1913.

3. Thibierge, G., and Weissenbach, A. J.: Concrétions calcaries souscutanées et sclérodermie, Ann. de dermat. et syph. **2**:129, 1911.

reported nine instances of calcinosis complicated with scleroderma, and Durham [1] collected the reports of thirteen additional cases from the literature, and reported one of his own. All of these were associated with scleroderma. In the reports of Weidman and Schaffer,[4] Maloney and Bloom,[5] and Bauer and co-workers [6] can be found an excellent review of the literature up to 1931. Since that time Craig and Lyall,[7] Shelley,[8] Kennedy [9] and Scholz [10] have each reported an additional case of calcinosis.

REPORT OF CASE [11]

History.—M. C., aged 56, married, was born in Italy, where she lived until 11 years of age. Since that time she had lived in California. Her past history revealed nothing of significance relative to her present complaint. No one in her family and none of her five children had a similar condition. The present illness began twenty years previously, when the patient observed hard nodules and plaques in the skin and subcutaneous tissues of the right side of the abdomen near the groin, the right groin and thigh. She could recall no injury to these parts and no preceding abnormality. During these twenty years the hardened areas continued to appear. Many of them eroded their way through the skin, discharging a chalky material. Frequently the lesions became inflamed and tender, and pus accompanied the discharge of this material. The presence of the deposits never caused the patient serious inconvenience.

Physical Examination (November, 1932).—The patient was well developed and well nourished, weighing about 130 pounds (59 Kg.). The head and scalp were normal. The pupils reacted to light and in accommodation. The ears, nose and mouth were normal except for the absence of teeth. The tonsils were hypertrophied and cryptic. No enlargement of the thyroid gland was noted. The heart and lungs were normal. The blood pressure was 142 systolic and 84 diastolic. The liver and spleen were not palpable. Arthritic changes were noted about the phalangeal joints of the fingers. The reflexes were normal. Pelvic examination gave negative results, except for the presence of a moderate rectocele and cystocele.

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4. Weidman, F. D., and Schaffer, L. W.: Calcification of Skin Including Epidermis in Connection with Extensive Bone Resorption, Arch. Dermat. & Syph. **14**:503 (Nov.) 1926.

5. Maloney, E. R., and Bloom, D.: Cutaneous Calcinosis, Arch. Dermat. & Syph. **23**:245 (Feb.) 1931.

6. Bauer, W.; Marble, Alexander, and Bennett, A. G.: Further Studies in a Case of Calcification of Subcutaneous Tissues (Calcinosis Universalis) in a Child, Am. J. M. Sc. **182**:237 (Aug.) 1931.

7. Craig, J., and Lyall, A.: Calcinosis Universalis, Suggested Method of Treatment, Brit. J. Child. Dis. **28**:29 (Jan.-March) 1931.

8. Shelley, H. J.: Calcification in the Subcutaneous Tissues, Arch. Surg. **23**:513 (Sept.) 1931.

9. Kennedy, R. L. J.: Calcinosis, Proc. Staff Meet., Mayo Clinic **7**:329 (June 8) 1932.

10. Scholz, T.: Calcification in Scleroderma, Am. J. Roentgenol. **28**:92 (July) 1932.

11. The opportunity of studying this patient was afforded through the courtesy of Dr. J. H. Bernard and Dr. Fred H. Zumwalt.

Local Condition.—The right thigh and abdomen presented an unusual picture. There were numerous hard indurated areas in the subcutaneous tissues of the skin extending from the middle of the back, radiating anteriorly in a fan-shaped fashion over the abdomen and right thigh. The plaques, about forty in number, varied from 0.5 to 2.5 cm. in diameter. Some were deeply seated, while others were near the surface. Several of the superficial plaques were elevated, and were purple. Many of the plaques and spicules had penetrated the skin, and a hard mass could be felt and seen through the small perforations thus formed. The skin over the plaques was slightly pruritic, but was not painful. Near these tumors the skin seemed leathery and hard and appeared to have a lessened resistance, as shown by the fact that when one of the lesions was removed the wound healed

Fig. 1.—Photograph of the right side of the abdomen and right thigh.

slowly, and secondary infection was invariable. Several large scars, the site of previous surgical removal of masses, were present.

The laboratory studies showed a slight elevation in the blood calcium, which was 12 mg. per hundred cubic centimeters of blood on two occasions. The blood phosphorus was 4.3 mg. per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were negative, and urinalysis gave negative results. The blood count showed 85 per cent hemoglobin, 4,320,000 red blood cells, 8,200 white blood cells, 75 polymorphonuclears, 11 large lymphocytes, 10 small lymphocytes, 2 transitionals and 2 eosinophils.

Qualitative analysis of some of the deposits in the skin demonstrated the presence of calcium salts.

Roentgen examination showed irregularly sized and shaped masses in the skin and subcutaneous tissues of the right side of the abdomen, right thigh and right arm.

Biopsy was done (see the pathologic report).

CLINICAL PICTURE

The various descriptions of calcinosis indicate that the clinical picture is not constant. The onset of the disease is insidious. Tumors or plaques varying in size from a pea to that of a walnut suddenly appear in various parts of the body, but usually under or in the skin. They are most frequently found on the hands, wrists, elbows, knees and the parts of the body most subject to trauma and muscular activity. These tumors may be either hard or soft in consistency, and are often brittle. The skin above the tumor may become red and inflamed, and by constant pressure may become perforated, the contents of the tumor being discharged at the surface. The tumor then disappears, often leaving a scar at the site of the lesion. New tumors appear, and the process is repeated. The condition is equally common among men and women, although in adults it is reported that more women are affected. Patients have varied in age from 5 weeks to 65 years.

Fig. 2.—Roentgenogram showing masses of calcium in the skin and subcutaneous tissues.

CHEMICAL COMPOSITION AND BLOOD CHEMISTRY

Maloney [5] stated that the composition of the plaques consists of a large amount of tricalcium phosphate, a trace of chlorides and a small amount of carbonates and organic matter. Calcium phosphates predominate (from 19.29 to 90 per cent), while calcium carbonate occurs

in lesser quantities (from 3 to 10 per cent). There is little change from normal reported in regard to blood calcium, phosphorus and cholesterol in these cases. It is generally estimated that from 9 to 11 mg. of calcium and from 3 to 7 mg. of phosphorus per hundred cubic centimeters of blood express the normal. Two hundred and fifty milligrams of cholesterol per hundred cubic centimeters of blood is considered the upper limit of normal.

The accompanying table shows the blood chemistry in a number of patients with calcinosis.

Blood Chemistry in Cases from the Literature

Author	Blood Calcium	Blood Phosphorus	Cholesterol
Tisdall and Erb: Am. J. Dis. Child. **27**: 28 (Jan.) 1924.....	9.7, 9.3	4.4, 4.5	
Weidman and Schaffer [4]	9.11, 11.8	....	188
Durham [1]	7.6	4.77	
Maloney [5]	8.4	6.35	202
Wilens and Derby: Am. J. Dis. Child. **31**: 34 (Jan.) 1926....	Normal	Normal	
Authors' case	12.0	4.3	
Shelley [8]	11.8	....	
Craig and Lyall [7]	10.2	3.92	
Kennedy [9]	10.8	4.2	

ASSOCIATION WITH OTHER DISEASES

Uncomplicated calcinosis is seldom found, but it is frequently associated with other diseases. As stated before, Weber, in 1878, recorded a case of calcinosis in association with scleroderma. Thibierge and Weissenbach [3] reported nine similar cases in 1911, and in 1928 Durham collected the reports of thirteen more cases from the literature and added one of his own. Langmead [12] and Tisdall and Erb [13] reported pronounced arthritic disturbances with marked limitation of motion in their cases. Langmead,[12] in addition, observed that calcinosis, generalized scleroderma, dermatomyositis and myositis fibrosa are intimately related. Jadassohn's [14] case was linked with osteomyelitis, causing the so-called "metastatic calcinosis." Chronic nephritis was the associated factor in the report of Weidman and Schaffer,[4] while Maloney's [5] case represented the metabolic type with an endocrine disturbance in addition to nephritis. Hunter [2] associated Raynaud's disease and arteriosclerosis with calcinosis.

ETIOLOGY

The etiology of calcinosis is unknown. Various theories have been offered. We have already advanced the theory of Langmead, who is of

12. Langmead, F. S.: The Relationship Between Certain Rare Diseases, Arch. Pediat. **30**:112, 1923.

13. Tisdall, F. F., and Erb, F. H.: Report of Two Cases with Unusual Calcareous Deposits, Am. J. Dis. Child. **27**:28 (Jan.) 1924.

14. Jadassohn, J.: Kalkmätastasen in der Haut, Arch. Dermat. u. Syph. **100**: 317, 1910.

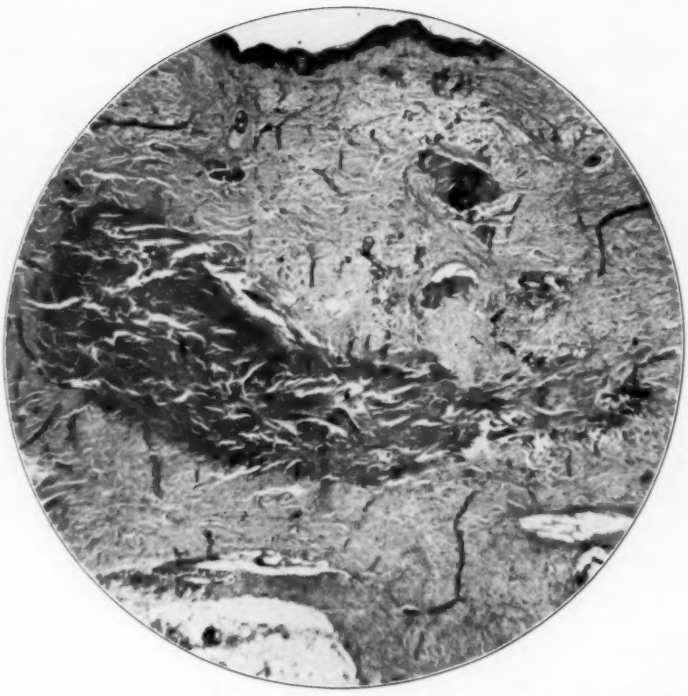

Fig. 3.—Photomicrograph showing masses of calcium in the derma and subcutaneous tissue; low power. Hematoxylin and eosin stain.

Fig. 4.—Photomicrograph showing swollen collagenous fibers merging directly with fibers within the calcified mass; high power. Hematoxylin and eosin stain.

the opinion that scleroderma, dermatomyositis, myositis fibrosa and calcinosis are manifestations of the same pathologic process, the nature of which is unknown. He does not consider these as entities in themselves. Hunter [2] regarded calcinosis as a complication of scleroderma. On the other hand, the studies of Bauer and co-workers [6] indicate that the disease is due to abnormal calcium and phosphorus metabolism. Tisdall and Erb [13] expressed the belief that it is a local condition and not a general metabolic change which is the factor determining the deposition of calcium salts. Again, Weidman and Schaffer [4] considered that calcification is a disturbance of fat metabolism in the epidermal cells, with the deposition of lime salts taking place secondarily to the fatty degeneration. Finally, Durham [1] questioned the function of the thyroid and parathyroid glands in the disease process, and the frequent association of nephritis suggested to him the possibility of some altered secretion causing chemical precipitation of calcium salts.

PATHOLOGY

In the case reported here a biopsy was done on one of the lesions of the right thigh. Gross examination of the tissue showed several irregular, thin, amorphous but rather firm, grayish-white, chalky areas, varying in size from that of about a pinpoint to 7 mm., within the subcutaneous tissue and extending upward into the derma.

The specimen was fixed in a dilute solution of formaldehyde, U. S. P. (1:10), Zenker's fluid and Bouin's fluid, and was decalcified by the nitric acid-phloroglucin method and by long immersion in Müller's fluid. Sections were then embedded in paraffin and stained with hematoxylin and eosin, Mallory's connective tissue stain, Giemsa's stain, von Kossa's silver method for staining calcium, Weigert's elastic tissue stain, and Unna's polychrome methylene blue stain (methylthionine chloride, U. S. P.).

Microscopic Examination.—Hematoxylin and Eosin Stain: The epidermis appeared normal. There was a slight amount of melanin pigment in the basal layer. The rete pegs varied in size and shape. In the corium the blood vessels were dilated and accompanied by a slight perivascular lymphocytic infiltration. An occasional arteriole about the calcified areas showed thickened walls and some hyalinization of the media. The hair follicles appeared normal. There was a moderate increase in the amount of fibrous tissue about the sebaceous glands. The coil glands showed a definite increase in the thickness of their basement membrane; otherwise their cells appeared normal. The erector pili muscles were prominent.

Extending throughout the corium were compactly arranged large, swollen, palely staining collagenous fibers. Among the collagenous bundles were several deeply staining homogeneous calcareous masses, which varied in size and were irregular in shape. These deposits were within the collagenous tissue, and in places could be seen to merge directly with these fibers.

The areas of calcification were for the most part acellular, but in one section there was an apparent attempt at bony transformation. In this place there were several small, vacuolated areas frequently containing two nuclei. No cartilage occurred.

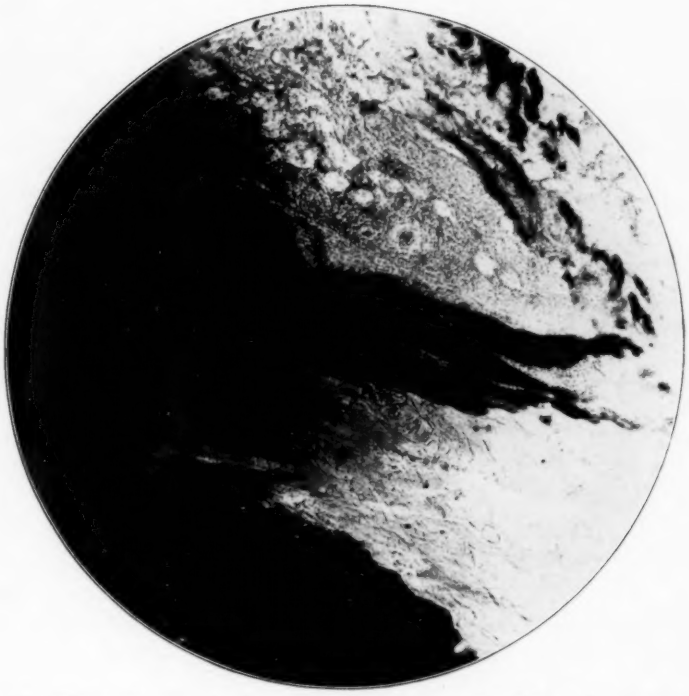

Fig. 5.—Photomicrograph showing black masses of calcium; low power. Von Kossa's silver nitrate stain.

Fig. 6.—Photomicrograph showing calcified masses with areolar tissue surrounding them; low power. Hematoxylin and eosin stain.

Fig. 7.—Photomicrograph showing a portion of the mass of calcium seen in figure 6, demonstrating an attempt at bone formation; high power. Hematoxylin and eosin stain.

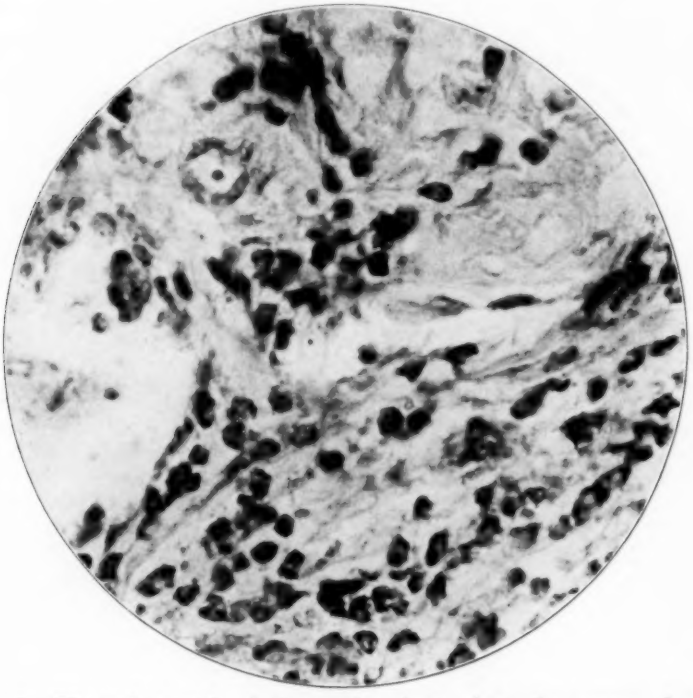

Fig. 8.—Photomicrograph of the areolar tissue about the masses of calcium as seen in figure 6; high power. Giemsa's stain.

There was a slight cellular reaction consisting of an infiltration of lymphocytes and a few plasma cells mainly about the vessels. Also, about the periphery of the calcified areas lymphocytes occurred in small foci. Here the stroma was of an areolar type, and mononuclear cells could be seen in its meshes. There were no giant cells present. No mast cells were seen after the use of Unna's polychrome methylene blue stain.

In the subcutaneous tissue the few blood vessels present showed a narrowing of the lumen, owing to thickening of the intima. Here also a moderate number of lymphocytes occurred in small foci, but this reaction was slight. The swollen collagenous fibers and the areas of calcification, as found in the corium, extended downward into the subcutaneous tissues.

Mallory's Connective Tissue Stain: With this stain the large swollen collagenous fibers stood out sharply. The thickened media of the blood vessels, the hyalinization and thickening of connective tissue about the sebaceous glands and the thickened basement membrane of the coil glands were made more evident. The calcified areas showed no tendency toward encapsulation.

Weigert's Elastic Tissue Stain: The elastic tissue appeared normal in character and distribution, but there was no direct connection between these fibers and the areas of calcification.

Giemsa Stain: No myelocytes were seen about the masses of calcium with this stain, demonstrating a lack of bone marrow formation.

Von Kossa's Silver Nitrate Method: The homogeneous masses in the corium reacted diffusely and strongly in the test for calcium.

TREATMENT

The treatment of calcinosis has been unsatisfactory. Yet the reports of Craig and Lyall [7] and Kennedy [9] are encouraging. The former authors caused a complete disappearance of the masses of calcium in their patient by administering disodium phosphate, 2 Gm. by mouth, three times daily. The last-mentioned author obtained a marked improvement in his patient by the use of a ketogenic diet. Bauer [6] advocated the use of a diet low in calcium combined with a decalcifying agent such as ammonium chloride.

PROGNOSIS

Calcinosis is not regarded as a grave condition, as it alone is not fatal. In the metastatic type, when there is marked destruction of bone the prognosis may be poor. When calcinosis is accompanied by another disease, such as leukemia, nephritis or scleroderma, the prognosis is that of the associated condition.

COMMENT

The case reported here presents the metabolic type of calcinosis, there being no disturbance in the normal depots of calcium in the patient's body. No associated disease is present which can be related to the calcified areas of the skin and subcutaneous tissues. There were no important changes in the blood chemistry except a moderate increase in the total amount of calcium.

The etiology of the condition is obscure, but the histologic investigation yields two important findings. The first is that the calcium is apparently deposited in the collagenous fibers. Swollen collagenous fibers suddenly change in their appearance owing to the deposition of calcium.

This observation is significant, as it indicates that the underlying process in this case is due to a disturbance of the collagenous material, probably of a physiochemical nature. The second finding is an area in the deposits of calcium where a suggestion of bony transformation has taken place. This tends to support the theory that true bony deposit in the skin is merely an advanced stage of calcification.

The frequent association of diffuse scleroderma with calcinosis is of particular interest and indicates possibly a common etiology. Thorough chemical investigations may show a close correlation between these conditions, or perhaps the sclerodermic process prepares the tissues for secondary deposits of calcium.

CONCLUSIONS

1. In a case of the metabolic type of calcinosis, the histologic changes indicate that the calcification took place in the collagenous fibers of the corium and subcutaneous tissues.

2. An attempt at a true bony transformation of the masses of calcium is suggested.

3. The frequent association of diffuse scleroderma and calcinosis may indicate a common etiology, or suggests that the sclerodermic process is preparatory for calcification.

GRANULOMA FISSURATUM, SUTTON (GRANULOMA TELANGIECTODES FISSURATUM)

REPORT OF A CASE

F. A. DIASIO, M.D.
NEW YORK

Recently, R. L. Sutton, Jr.,[1] reported two instances of a fissured granulomatous growth in the mouth situated in the superior labio-alveolar sulcus. Both cases occurred in women, and in both the small solitary tumors had been present for several weeks and had persisted without any marked increase in size during that period.

The histologic structure of the two lesions was practically identical. The epidermis was acanthotic and bisected by a deep fissure, at the bottom of which a wedge-shaped tongue of connective tissue separated the ends of the epidermis. In the cutis there were a marked proliferation of connective tissue, a cellular infiltration in which polymorphonuclear leukocytes predominated and numerous new blood vessels.

A third case, which also occurred in a woman, aged 43, has since been reported by R. L. Sutton.[2] The clinical features and the pathologic findings did not differ from those just described.

In April, 1933, there appeared in my clinic an old man, whose case I shall describe.

REPORT OF CASE

The patient was a widower, 67 years old, retired, who had been born in Italy. He had no history of venereal disease. After the age of 40, he began to lose his teeth, one by one; five years before I saw him he had the few remaining pegs extracted. His dentist furnished him with a set of false teeth which was so ill-fitting that when he ate soup or other liquid foods, the denture invariably slipped out of his mouth. Six months before his admission to the clinic he discarded the annoying contraption because "the plates interfered with his eating."

Three months before admission, he noticed a burning of the tongue during meals. About one month before readmission he observed a small lump to the right of the frenum in the lower labio-alveolar sulcus. Fearing that it might be cancer, he decided to seek consultation.

From the Department of Dermatology and Syphilology, Columbus Hospital, service of Dr. F. A. Diasio.

1. Sutton, R. L., Jr.: A Fissured Granulomatous Lesion of the Upper Labio-Alveolar Fold, Arch. Dermat. & Syph. **26**:425 (Sept.) 1932.

2. Sutton, R. L.: Granuloma Fissuratum, Arch. Dermat. & Syph. **26**:865 (Nov.) 1932.

Examination revealed an emaciated, old man. The skin was normal except for senile changes. Dr. Gallo, in making an ocular examination, found an old trachoma with secondary entropion and incipient senile cataracts. Dorsal scoliosis, an emphysematous chest and bilateral indirect inguinal hernia were also found.

The mouth was edentulous. The oral mucosa, tongue and palate did not show any abnormalities. To the right of the frenum of the lower labio-alveolar sulcus there was a biscuit-shaped tumor, the long axis of which was parallel with the labiomaxillary groove. It measured approximately 0.6 by 1.2 cm. and was raised about 4 mm. from the general level of the coronal plane. Its oval top was somewhat flattened. A deep longitudinal indentation bisected the growth so that its shape suggested "that of a folded coin, the indentation being within the bend" (fig. 1).

The granulomatous lesion was smooth and glistening and had a pearly-white tint rather than the pale pink color noted by the Suttons. The borders were sharply raised and smoothly rounded. There was no bright red, narrow line (fissure) across the center, for the indentation was also pearly white.

Fig. 1.—Note the location and appearance of the granuloma.

The tumor was firm and solid to the touch, not as hard as an epithelioma might be, and of about the same consistency as granuloma telangiectodes. There was no tendency to bleeding on manipulation, and no inflammatory areola was present. The solitary mass was painless. Notwithstanding the fact that its base was not infiltrated, it was but slightly movable over the alveolar process of the underlying maxillary bone.

The Wassermann test and other routine laboratory investigations gave negative results. The tumor was excised under local anesthesia, and sections were prepared and stained in the Dermatological Laboratories of the New York Post-Graduate Medical School and Hospital (courtesy of Prof. G. M. MacKee).

The pathologic report that follows was made by Prof. J. Frank Fraser:

"The specimen consists of epidermis and corium (fig. 2). The epidermis is indented in the middle and the indentation contains masses of corneous cells (fig. 3). The shapes of these cells are visible, but nuclei are not present. The corneous masses are extensively infiltrated with red cells and hemolytic serum. The corneous surface of the whole specimen is broken up into pools of serum and fibrin over which is a compact layer of red cells and necrotic débris. The epidermis itself is very thick, the pegs being long and cellular (acanthosis). The prickle

Fig. 2.—Note the central indentation and the symmetrical halves of the tumor.

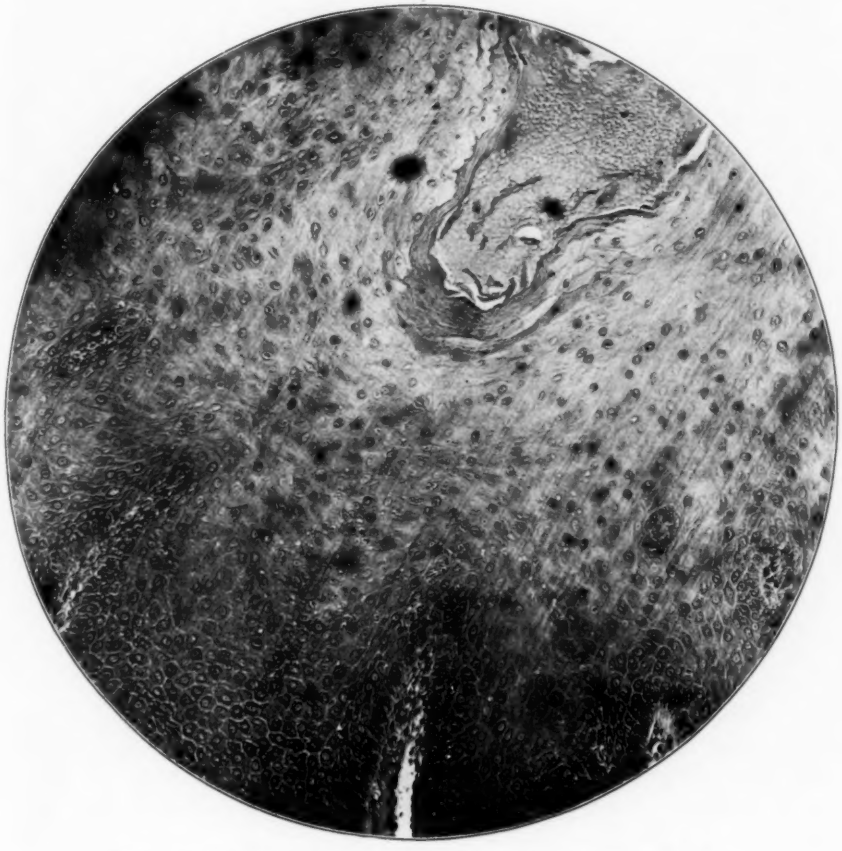

Fig. 3.—The indentation contains masses of corneous cells.

cells show a thick outer layer. They are hydropic and gradually pass into the corneous layer described above. In places, masses of homogeneous hyaline material can be seen.

"The corium shows a large number of apparently new vessels with a moderate lymphocytic and plasma cell infiltration around them (fig. 4). The collagen fibers are pale-stained, very much swollen and fused into homogeneous hyalinized tissue (fibrosis).

"The histologic diagnosis is fissured, hyperplastic granuloma."

Fig. 4.—There are many new vessels, surrounded by a moderate infiltration of lymphocytes and plasma cells.

COMMENT

Apparently my case is an example (the fourth reported) of granuloma fissuratum. It differs from the previous cases recorded in that (1) my patient was a man, (2) the lesion occurred in the lower labio-alveolar groove (in contradistinction to R. L. Sutton, Jr.,'s cases in which the solitary masses were situated in the superior labio-alveolar mucosal fold), and (3) unlike R. L. Sutton's third case in which the

granuloma was located on the left side of the frenum, the tumor was to the right of the frenum.

In addition to the gross features mentioned, it is striking that my sections indicate the early changes that occur in granuloma fissuratum and thus furnish, in my opinion, a clue as to both the development of the growth and its nosologic status.

A study of my specimens has convinced me that the microscopic changes of so-called granuloma fissuratum are identical with those usually considered typical [3] of granuloma telangiectodes. Moreover, I believe that Sutton's granuloma develops as follows: Owing to the mechanics of the situation (either labio-alveolar groove) and the looseness of the tissues on both sides of the fixed sulcus, the epidermis is lifted on either side of the coronal plane as the fissured granuloma begins to develop. Thus an indentation (noted in my specimens) is formed in the center of the lesion. On account of the out-of-the-way location of the fissured granuloma at the apex of the sulcus, not only are attempts to heal this condition once it has begun to develop frustrated by the continued irritation of decaying food particles lodged in the vestibulum oris near the frenum where they are hard to remove with the tongue, but eventually the indentation produced also breaks down, causing loss of continuity of the epidermis and subsequent formation of the fissure. Once the barrier of epidermic cells is gone and secondary infection of the open lesion supervenes, the formation of the wedge-shaped tongue of connective tissue and the appearance of polymorphonuclear leukocytes are the natural sequences of the bacterial invasion. On the other hand, a similar lesion (i. e., granuloma telangiectodes) elsewhere is free to develop, so that the entire epithelium is readily lifted up by the proliferating tissue of the cutis in the form of an oval or spherical mass to give rise to the typical clinical picture of granuloma telangiectodes without indentation or fissuring.

CONCLUSIONS

1. Granuloma fissuratum of Sutton is not a clinicopathologic entity *sui generis* but is rather a clinical variety of granuloma telangiectodes, its special characteristics being due to the location of the lesion.

2. The fundamental lesion is not, pathologically speaking, the fissure, for this may not always be present.

3. The condition may develop in either labio-alveolar sulcus and to the right or the left of the frenum.

4. The designation "granuloma telangiectodes fissuratum" is to be preferred to Sutton's appellation.

5. A fourth case, which occurred in a man, is recorded.

19 East Ninety-Eighth Street.

3. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 225.

SELF-STERILIZING POWERS OF THE SKIN

V. ARE THEY ENDOWED BY THE SURFACE ACID?

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CHICAGO

In a previous study [1] it was shown that the skin arrests the activity of micro-organisms on its surface. In a later report [2] this restraining capacity of the skin was shown not to be uniform, but to be subject to constant fluctuations. These fluctuations can be brought about in numerous ways, the degree of the variation from the optimal depending on the specific method or agent used. The sterilizing process, therefore, is sensitive to both internal metabolic and environmental changes. In discussing the data, it was postulated that whatever upsets the equilibrium of the skin causes the self-sterilizing powers to sag for the moment until compensation for the previous change occurs. It was felt that there was no choice but to assume some such mechanism, because agents of opposite physiologic action all gave rise to the same immediate qualitative results. Of course, as was stated, it would be desirable to know what ultimately is responsible for sterilizing the skin. One could then study this isolated factor to see how it varies under different conditions to change the sterilizing capacity.

Just such a factor has been reported by various authors to be responsible for sterilizing the skin. This factor is said to be the acid of the surface. This communication will, therefore, concern itself with a critical examination of the reports of these authors as well as with a description of original experiments designed to test the validity of their hypothesis.

According to Schade and Marchionini,[3] the reaction of the surface of the skin differs from that of the sweat. They cited E. Heuss as stating that the surface reaction does not depend on the sweat reaction but is a characteristic of the skin *sui generis*. These authors found a reduction in acidity with the appearance of freshly secreted sweat and an increase in acidity on its evaporation. They thought that the

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From the Department of Dermatology, University of Illinois, service of Dr. F. E. Senear.

1. Cornbleet, T., and Montgomery, B. E.: Self-Sterilizing Powers of the Skin, Arch. Dermat. & Syph. **23**:908 (May) 1931.

2. Cornbleet, T.: Self-Sterilizing Powers of the Skin: IV. Action of Drugs and Hormones, Arch. Dermat. & Syph. **27**:756 (May) 1933.

3. Schade, H., and Marchionini, A.: Der Säuremantel der Haut, Klin. Wchnschr. **7**:12, 1928.

acidity of the sweat decreased with beginning evaporation, owing to the early loss of highly volatile acids, and then definitely and persistently increased. They found, further, that if fresh sweat is not soon concentrated by evaporation, it disintegrates and forms ammonia as a result of contact with the epithelial cells and the action of micro-organisms. They noted disintegration of weakly acid sweat in from five to seven hours and suggested that certain areas of the body where evaporation of the sweat is hindered have a tendency to become diseased.

Herrmann and Fürst [4] used sweat baths therapeutically in a number of disorders of the skin with good results. They found that, regardless of the method used to induce sweating, the end-results were the same. They, too, found that fresh sweat was more alkaline than that which is allowed to evaporate. Among other dermatoses they were able to cure mycotic infections by means of sweating.

Marchionini and Ottenstein [5] cited Talbert's, as well as their own, work in concluding that it is the evaporation of the moisture from sweat which forms a thin, physiologic, but very important, layer, or as they termed it, "acid cloak," about the skin. This layer, they say, destroys the micro-organisms on the skin by means of its bactericidal ability. They explain that every sweat bath causes a regeneration of the acid cloak and thereby destroys the bacterial and mycotic disease organisms. They believe that by means of this first line of defense one can explain the beneficial activities of sweat baths in skin diseases of bacterial-mycotic origin.

For purposes of later analysis it may be well to discuss Schade and Marchionini's observations at length. They said that the acid cloak of the skin has the highest acid values in the human body except the gastric secretion in adults. That this acid cloak has a very important antibacterial protective power is, therefore, not to be doubted. This is in accord with the discovery of Koch, Zangemeister, Grutz and others, who showed that one rarely finds pathogenic organisms on the normal skin. They cite the observation of Noguchi, that virulent organisms, if placed on the normal skin, become saprophytic in a short time. They go on to say that the acidity of the skin is not the same in all regions of the body, some areas, such as the axilla, having a comparatively alkaline reaction. Because every sweat brings with it a reduction of the acidity of the surface of the skin, the regions which are characterized by much sweating have a lower acidity and therefore a lower protecting power. All cuts or erosions of the skin cause a loss of the acid protection. As

4. Herrmann, F., and Fürst, K.: Ueber Schweiss-Secretion und ihre Bedeutung bei Dermatosen, Dermat. Wchnschr. **88**:397, 1929.

5. Marchionini, A., and Ottenstein, B.: Neuere Untersuchungen über die Wirkung von Schwitzbädern, Therap. d. Gegenw. **72**:389, 1931.

soon as the epidermal layer over even the smallest area is removed, the acid cloak, the purpose of which is to protect against bacterial invasion, is broken down. This gives rise to a reaction which is the optimum for the growth of many bacterial invaders. Similar defects in the acid protection must occur in regions where the stagnating sweat can become alkaline; this probably is not an unimportant factor in the regional disposition to skin diseases. It should be observed that the body uses the same means of protection against bacteria in three regions as different as the stomach, the vagina and the skin.

Levin and Silvers [6] stated that they found that under normal conditions the reaction of the surface of the skin is acid, having a p_H of from 5 to 5.5, and on that account inhibits the growth of bacteria and fungi. To combat the changed reaction of the sweat on the feet, which makes the region of the toes favorable for the growth and multiplication of fungi, they had been using 1 per cent of salicylic acid in talcum powder in interdigital maceration and scaling as a prophylactic measure.

EXPERIMENTS

It has been known for a long time that sweat in vitro is a good medium for the growth of bacteria. I shall cite here some experiments in confirmation of this.

Sweat was collected from persons in a heat chamber. Samples were plated immediately and each day thereafter from material kept in the icebox and incubated at 37 C. In some cases the sweat was boiled to obtain sterility. Some of the latter material was inoculated with a definite amount of staphylococci, and the growth of this known amount of inoculum was observed from day to day. Sweat was allowed to evaporate and concentrate to various degrees—three-fourths, one-half and one-fourth—and then inoculated with staphylococci. Observations were made on the growth of yeast and staphylococci in sweat kept buffered at a p_H ranging from 3 to 8. All these observations were repeated with the addition of keratin. Other control studies were made with plain buffered solutions and buffered solutions containing salts in the same proportion that I found them in a chemical analysis of sweat. In another set of experiments material from all the preparations just described was spread on the skin, and the effect on recoverability of the contained micro-organisms was noted. In the latter experiments the micro-organisms disappeared, though with varying degrees of rapidity (that is, minutes), whereas when left in the test tubes in plain sweat or any of its modifications they remained viable indefinitely. On the more acid areas of the skin the protection was a little more effective, but not significantly so. The relatively alkaline areas also were able to sterilize themselves though they required a slightly longer time.

In still another set of experiments, the reaction of the skin surface was observed under the influence of various acids. With highly buffered acids of low dissociation,

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6. Levin, O. L., and Silvers, S. H.: The Possible Explanation for the Localization of Ringworm Infection Between the Toes, Arch. Dermat. & Syph. **26**:466 (Sept.) 1932.

such as boric acid, it was found that, while the skin surface became more acid for a time, invariably after the third day the reaction swung more and more toward the alkaline side, notwithstanding continued contact with the acid reagent. Frequently after several days' contact with such an acid reagent the surface was more alkaline than before its use. With highly dissociated acids, such as hydrochloric acid, the skin surface could easily be given a more acid reaction. Under continued application of the hydrochloric acid the skin was irritated, in practically all cases, even when concentrations as low as hundreth-normal were used. Further, unless dressings of considerable bulk were applied, the surface of the dressing was quickly neutralized.

In a publication elsewhere on sweat the detailed quantitative results of these experiments will be reported. In this paper I shall give merely qualitative results. These showed that sweat and its modifications are excellent mediums for the growth of yeast and staphylococci, even at a p_H as low as 3.

COMMENT

The various authors have assumed that because the chemical reaction of the surface of the skin is acid and the surface is endowed with antibacterial properties, the two phenomena are necessarily related. Some have made the suggestive comparison that the stomach and vagina also have acid reactions, for the purpose, among others, of destroying bacteria. One is therefore led to believe that these organs have another method of sterilizing themselves than that in use at other more alkaline levels of the alimentary canal or on such surfaces as the conjunctivae. I am unaware that in any of the reports there is proof of a relationship between the two processes. Without such proof the conclusions represent *post hoc, ergo propter hoc* reasoning. While one would not want to deny that the maintenance of an acid reaction on the surface of the skin is purposeful, it is not necessarily for destroying micro-organisms. No facts have been brought forward to warrant such a conclusion, nor do my experiments justify it.

Every clinician of experience is familiar with the fact that the skin has powers of acclimation to various medicinal agents. Those which have been used with initial good effects often lose their powers and must be replaced sooner or later if they are used for a chronic disorder. It is not surprising, therefore, that in these experiments it was found that such agents as boric acid could not be counted on for long to influence the reaction of the skin. One learns after studying the chemical constitution of the skin that it is tenacious in keeping its given make-up and exceedingly rebellious toward even small changes, and that while some changes may be made for a time, the skin soon learns to overcome the weaker reagents used to influence it. On the other hand, if these reagents are strong, they irritate the skin. For this reason, as was

found in the clinical experiments reported, one often does ill in using such an agent as boric acid to increase acidity because an end-result of relative alkalinity is brought about that is difficult to influence. Salicylic acid has been proposed to increase the acidity. It, however, is a very weak acid, the number of hydrogen ions it furnishes being limited. On the other hand, it possesses marked fungicidal properties. Whatever therapeutic value it would have would be due to the molecule as such and not to the hydrogen ions it furnishes. A better known prototype of its action is found in phenol, which has bacteriostatic value, not because of its acid make-up, but because of its specific and peculiar molecule as a whole. In the case of hydrochloric acid, which has been recommended in the form of wet dressings, it is assumed that an acute process is present. One would not prescribe the use of awkward wet dressings for preventive purposes in regions of relative alkalinity, such as the axilla. Nor would we recommend them in a chronic condition, say, in eczematoid ringworm. Their use for prevention or in chronic processes would be unpractical. In eczematoid ringworm of the subacute type I have found them not only not beneficial, but irritating. For purely chemical reasons alone it is entirely irrational to employ unbuffered materials, such as hydrochloric acid. First, large amounts of the material must be used if it is to remain active for any length of time, and second, the full impact of its influence is felt at once as a maximum blow and it therefore proves irritating. An example of how the body economy finds it necessary to use buffers in maintaining its acid-base equilibrium is found in the elaborate buffering mechanism in the blood. A more rational procedure than the use of hydrochloric acid for the maintaining of a given reaction on the skin with chemical agents would be to employ materials that are buffered and yet have a moderate dissociation constant, such as the phosphates. But even were these successful in achieving and maintaining a desirable acidity on the skin surface, there is no assurance that the skin would thereby be improved in its capacity to inactivate micro-organisms. My experiments show that micro-organisms do not grow quite as well in sweat of a higher acidity as in sweat of a lower acidity; none the less, samples of a high acidity, that is, of a p_H of 3, supported a luxurious growth. The experiments also showed that the skin could inactivate staphylococci even though its surface reaction was kept neutral at a p_H of 7.

SUMMARY

1. Several authors have attributed the self-sterilizing powers of the skin to its surface acid and have advocated therapeutic measures based on this hypothesis.

2. They have done this without presenting direct or indirect proof that the acid itself is a bacteriostatic agent.

3. Original experiments designed to test the validity of their contentions are reported.

4. Theoretical and clinical objections to their therapeutic measures are discussed.

CONCLUSION

There is no proof in the literature nor do my experiments support the hypothesis that the self-sterilizing powers of the skin are due to the surface acid.

YEASTLIKE FUNGI FOUND ON THE SKIN AND IN THE INTESTINES OF NORMAL SUBJECTS

A SURVEY OF ONE HUNDRED PERSONS

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The etiologic relationship of fungi recovered from the skin to the lesions in which they are found is a problem of interest to dermatologists. Organisms generally referred to as moniliae or oidia are regularly found in erosio interdigitalis, in perlèche, in a well defined type of paronychia and in diabetic intertrigo. Two opinions are held in regard to them: one, that the fungi are the cause of the lesions in which they occur; the other, that they are saprophytes which find the diseased skin a favorable soil. The fact, previously reported,[1] that most of these organisms belong to one well defined species (Monilia albicans) substantiates the idea that these lesions are a specific infection—moniliasis of the skin.

Doubt is still thrown, however, on the etiologic importance of M. albicans by the fact that organisms not differentiated from this species by observers are frequently encountered on normal skin.

In 1922, Greenbaum and Klauder,[2] in a study of yeast infections of the skin, reported a survey of normal skins for yeastlike fungi. From 150 patients they recovered thirty-five strains. They believed that both the strains which they isolated from erosio interdigitalis and those from normal skin were saccharomycetes or cryptococci. With a strain from normal skin identified as a cryptococcus they produced a lesion on an abraded finger web. They concluded: "Yeasts which are found normally on the skin may under certain conditions become pathogenic and cause a superficial infection." Jessner and Kleiner [3] reported similar

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1. (*a*) Benham, R. W.: Certain Monilias Parasitic on Man, J. Infect. Dis. **49**:183 (Sept.) 1931. (*b*) Hopkins, J. G.: Moniliasis and Monilids, Arch. Dermat. & Syph. **25**:599 (April) 1932. (*c*) Robinson, L. B., and Moss, M. C.: Superficial Glossitis and Perlèche Due to Monilia Albicans, ibid. **25**:644 (April) 1932.

2. Greenbaum, S. S., and Klauder, J. V.: Yeast Infections of the Skin, Arch. Dermat. & Syph. **5**:332 (March) 1922.

3. Jessner, M., and Kleiner, S.: Arch. f. Dermat. u. Syph. **149**:363, 1925.

findings. They obtained yeastlike fungi from cultures of fingernails of 60 per cent of normal persons examined, and with these cultures produced interdigital erosions on finger webs which had previously been macerated. More recently, Staehelin, Mu and van Schouwen [4] published an important study of the whole question of oidiomycosis (moniliasis). They made cultures from 120 persons, 64 of whom had normal skins and 56 various dermatoses. Yeastlike fungi were recovered from 77.5 per cent (positive cultures were slightly more frequent from the normal persons than from those with diseased skin). The number of cultures obtained from various areas was as follows: head, 20 per cent; chest, 30 per cent; fingernails, 27.5 per cent; toes, 50 per cent, and lower part of the leg, 28 per cent. A comparison was made of two of these strains from normal skin and a number of strains isolated from various types of moniliasis. Slight differences were observed, and the illustrations showed that the normal strains when grown on maltose agar lacked the coral-like formation seen in the center of the colonies in most of the strains from diseased skin. They also lacked the filamentous outgrowths which appeared around the colonies of most of the latter strains when grown on acetic acid agar. These differences seemed more quantitative than qualitative and depended on the medium and the age of the culture. The authors concluded that the distinctions were neither so constant nor so fundamental as to justify the separation of the strains into different species. At the same time, they emphasized that differentiation and identification of the cultures are not only useful, but a necessary prerequisite for the determination of the rôle of microorganisms in the causation of disease.

Other investigators have reported somewhat different results. Falchi,[5] in cultures from the nails of 45 persons, obtained yeastlike fungi from only 4. Ravaut, Rabeau, Longhin and Sloimovici [6] obtained yeasts in only 13 of 150 persons studied. Wachowiak, Stryker, Marr, Bock and Fleisher [7] failed to find Monilia in the skin of 25 normal persons or in the blood of 24 when cultures were made. On the other hand, Monilia was found in the stools of 6 of 100 normal persons and in those of 40 per cent of patients with persistent diarrhea. The presence of other yeastlike types was not recorded.

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4. Staehelin, A.; Mu, J. W., and van Schouwen, M.: Arch. f. Dermat. u. Syph. **165**:294, 1932.

5. Falchi, G.: Arch. f. Dermat. u. Syph. **152**:427, 1926.

6. Ravaut, P.; Rabeau, H.; Longhin and Sloimovici: Bull. Soc. franç. de dermat. et syph. **36**:607, 1929.

7. Wachowiak, W.; Stryker, G. V.; Marr, J.; Bock, H., and Fleisher, M. S.: The Occurrence of Monilia in Relation to Psoriasis, Arch. Dermat. & Syph. **19**: 713 (May) 1929.

If it is true that the same fungus found regularly in so-called moniliasis is frequently present on normal skin, the significance of finding it in lesions becomes doubtful.

The main purpose of the study to be reported was to approach this problem again with the aid of the newer methods which have been developed for the identification of M. albicans [1a] and to determine whether this apparently pathogenic fungus does occur frequently on the normal skin.

A similar problem has arisen in the investigation of tropical sprue. Kohlbrügge,[8] Ashford [9] and others have described the presence of M. albicans (psilosis) in the intestines of patients with tropical sprue, but the etiologic relationship of the parasite to this disease has been in doubt because apparently similar fungi occur frequently in the normal intestines.

Anderson [10] stated that in a study of 175 persons he found an organism corresponding to M. psilosis in only 1. This patient had the clinical history and symptoms typical of sprue. Nye,[11] on the other hand, found an organism similar to M. psilosis, which he termed Parasaccharomyces A, in the intestines of persons suffering from a variety of diseases, such as pernicious anemia, gastric achylia and mild intestinal disorders. He concluded that M. psilosis is unimportant as an etiologic factor, not only in pernicious anemia, but also in sprue. Wachowiak's findings have already been mentioned. Ashford [12] reported that 5.6 per cent of 178 healthy boys examined were found to be carriers of M. psilosis as against 52.7 per cent of 74 patients with sprue.

On account of these reported observations, it seemed important to include cultures from the tongue and from the feces in the present survey to determine whether M. albicans occurs with any frequency in the intestines of normal persons.

It is, however, not only with M. albicans that dermatologists are concerned. Other simple fungi, mostly belonging to the genera Cryptococcus and Mycoderma, have been found by many observers in lesions of the skin, and etiologic importance has been attributed to them without making clear whether these forms differ in any way from fungi occurring on normal skin. For example, MacLeod and Dowling [13] have

8. Kohlbrügge, J. H. F.: Arch. f. Schiffs- u. Tropen-Hyg. **5**:394, 1901.

9. Ashford, B. K.: Am. J. M. Sc. **154**:157, 1917.

10. Anderson, H. W.: J. Infect. Dis. **21**:341, 1917.

11. Nye, R. N.; Zerfas, L. G., and Cornwell, M. A.: Am. J. M. Sc. **175**:153, 1928.

12. Ashford, B. K.: Mycology of Intestinal Canal in Porto Rico and Its Relation to Tropical Sprue, J. A. M. A. **93**:762 (Sept. 7) 1929.

13. MacLeod, J. M. H., and Dowling, G. R.: Brit. J. Dermat. **40**:139, 1928; **42**:549, 1930.

recently reported finding regularly a cryptococcus called "Pityrosporon of Malassez" in the lesions of seborrheic dermatitis. No clear criteria have been established, however, to enable one to differentiate this organism from other cryptococci of the skin. C. J. White and J. H. Swartz [14] described a condition which they called cryptococcosis epidermica, in which they reported finding cryptococci, and Cleveland White [15] also found in eczematous lesions cryptococci with which he was able to reproduce the picture of the disease in the patients from whom they were obtained. It would be impossible in this report to detail all the reports of diseases in which the finding of cryptococci has been believed by the authors to be of significance.

In addition to moniliae and cryptococci one encounters in cultures from normal skin fungi in which the mycelium breaks up into rounded or oblong arthrospores. These spores, when isolated, resemble somewhat the yeasts, though as a rule they develop no buds. They are called by some authors mycodermata, and by others oidia. Instances have been reported of infection by fungi of this group.

Babes, in 1882,[16] cultivated a parasite which he called Oidium subtile from a patient who presented small ulcers on the abdomen and thigh. He reproduced the lesions in rabbits by injections of the organism. Another case was that reported by de Beurmann, Gougerot and Vaucher.[17] Clinically the disease resembled sporotrichosis, but from a number of closed lesions a fungus was isolated to which the name Mycoderma cutaneum was given. This was described as showing budding forms in young cultures, but later developing long filaments which broke up into chains of thick-walled cells. Similar parasites have been isolated from sputum in cases of chronic bronchitis by Castellani and others.

In view of these facts it seemed worth while to study the occurrence in normal persons not only of M. albicans and other moniliae, but of cryptococci and mycodermata as well.

METHODS

Cultures were obtained from 100 apparently normal young adults.[18] The condition of their skin was noted, and no eruption was found except a slight scaling between the toes in 31. Some of these persons gave a definite history of ringworm. Cultures of Trichophyton or Epidermophyton were obtained from 6. Specimens

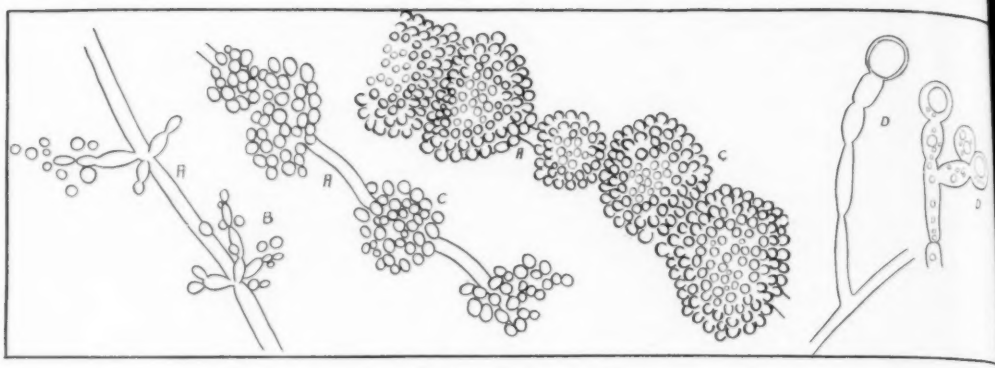
14. White, C. J., and Swartz, J. H.: Cryptococcosis Epidermica, Arch. Dermat. & Syph. **18**:692 (Nov.) 1928.

15. White, Cleveland: New York State J. Med. **27**:1116, 1927.

16. Babes, V.: Biol. Centralbl. **2**:569, 1882.

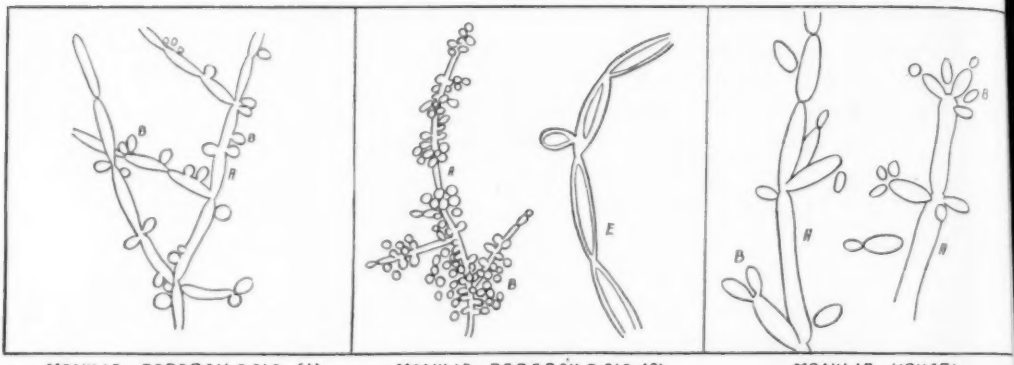
17. de Beurmann, Gougerot and Vaucher: Rev. de méd., Paris **30**:397, 1910.

18. This group included a number of students of the College of Physicians and Surgeons and student nurses from the Presbyterian Hospital. The greatest number of volunteers were from the freshman class of Columbia College.



MONILIA ALBICANS

Mycelium (A) Budding cells (B) Clusters (C) Chlamydospores (D)



MONILIA PARAPSILOSIS (1)

FROM NORMAL SKIN

Mycelium (A) Budding cells (B)

MONILIA PARAPSILOSIS (2)

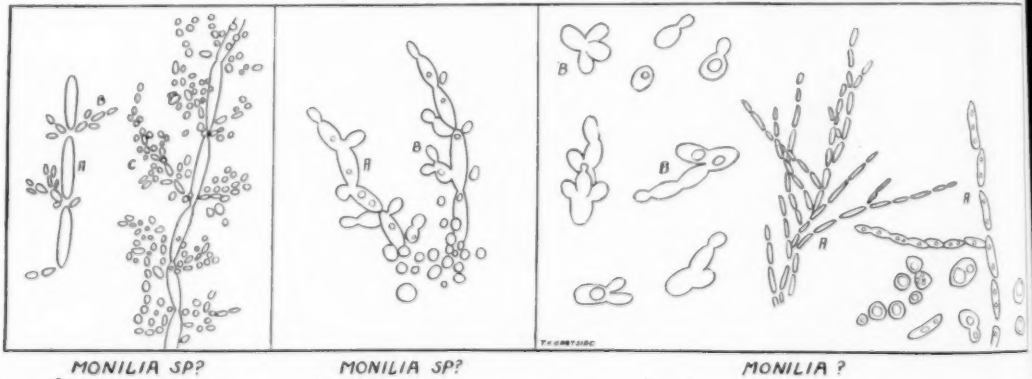
FROM FECES

Mycelium (A) Budding cells (B) Giant mycelium (E)

MONILIA KRUSEI

FROM NORMAL SKIN

Mycelium (A) Budding cells (B)



MONILIA SP?

Strain 1 from normal skin

Mycelium (A) Budding cells (B)

Irregular clusters (C)

MONILIA SP?

Strain 2 from normal skin

Mycelium (A) Budding cells (B)

MONILIA ?

Strain 3 from normal skin

Mycelium (A) Budding cells on honey agar

Monilia albicans contrasted with other species of Monilia. Morphology on corn-meal agar; magnification about 700.

were taken from the following locations: (1) the skin and nails of the fingers, (2) the web between the fourth and fifth toes, (3) the nail of the great toe, (4) the surface of the tongue and (5) the feces.

The middle finger of the right hand was placed in a small tube containing honey broth and kept there for five minutes. Scrapings were then made of the nail and skin at the base of the nail directly into the broth. Dilution plates of agar were made from the broth so inoculated. The nails and webs of the toes were scraped with a sterile scalpel and the scrapings planted directly on honey agar slants. Material was obtained from the tongue by scraping with a scalpel and similarly inoculated. Cultures from the feces were made by the contact plate method of Ashford. The p_H of each specimen of stool was determined colorimetrically at the same time that the cultures were made. The strains isolated were purified by making dilution plates and fishing isolated colonies. The form of the giant colonies on plates of honey agar was observed. Slit cultures were made on plates of cornmeal agar for the study of the morphology. Fermentation tests were made in Dunham tubes in 1 per cent peptone water containing 1 per cent dextrose, levulose, maltose, saccharose and d-galactose respectively, with litmus as an indicator. Agglutination tests were made with all strains which formed satisfactory emulsions in rabbit serums prepared against M. albicans, M. candida, M. parapsilosis, M. krusei, Cryptococcus, group I, and Saccharomyces cerevisiae.

Additional agglutination tests made in an effort to classify the cryptococci will be described in a later report.

Mold fungi, such as Aspergillus and Penicillium, were obtained in great numbers. These forms are being studied by Dr. B. O. Dodge and will be made the subject of a separate report.

CLASSIFICATION OF ORGANISMS OBTAINED

The so-called yeastlike fungi recovered in this survey were chiefly representatives of three groups:

1. The moniliae: Forms producing a pasty, cream-colored growth and both mycelium and budding cells in culture.

2. The cryptococci: Forms producing a cream-colored, yellow, tan or pink, pasty or mucoid growth and budding cells only, in culture.

3. The mycodermata: Forms producing dry corrugated, or flat downy growths and a definite septate mycelium of oblong cells which break up into spores, the arthrospores.

THE MONILIAE

The criteria by which the moniliae most frequently encountered may be recognized have been described in full in a recent publication.[1a] The differential key given in table 1 may be found helpful. The fermentation and agglutination reactions of M. albicans, parapsilosis and krusei are shown in table 2. In these reactions M. candida differs from M. albicans only in the production of gas in saccharose.

M. Albicans.—We were chiefly concerned with the occurrence of M. albicans in normal persons. In routine diagnostic work we have not encountered this species on the skin except in lesions of which it was apparently the cause. In this survey, as appears in table 3, M. albicans was not recovered from the skin or nails in any case, but was

found in the alimentary tract in 18 cases. Forty-three strains obtained from these cases produced characteristic giant colonies, formed spore clusters and chlamydospores on cornmeal agar and fermented dextrose, levulose and maltose with the formation of gas. Some strains also produced acid and gas in d-galactose and acid in saccharose. They agglutinated in the serum prepared against M. albicans to practically the full titer and also in the serum prepared against M. candida. They showed a varying degree of agglutination in the other serums used but usually less than the homologous strains.

M. Parapsilosis.—Two strains from skin and two from the feces showed the main cultural and morphologic characteristics of M. para-

TABLE 1.—*Differential Characteristics of Moniliae Most Frequently Found in Skin and Intestines*

	Pathogenicity for Rabbits	Colony	Budding Forms	Mycelium	Other Characteristics
M. albicans....	+	Cream-colored greenish tinge, pasty, raised growth, often with ruptured air bubbles near center	Oval; size, 5 to 6 by 3 to 4 microns	Well developed	Chlamydospores and spherical spore clusters; buds usually at ends of mycelial segments
M. candida.....	0	Cream-colored to tan, membranous, much convoluted	Oval; size, 6 by 3 to 4 microns	Well developed	Chlamydospores rare; no spherical spore clusters; buds anywhere on mycelium
M. parapsilosis	0	Cream-colored, pasty, often honey-combed	Oval; size, 4 to 5 by 3 to 4 microns	Fragile, abundant, branching	Occasional "giant" filaments; irregular spore clusters; buds usually at ends of mycelial segments
M. krusei.....	0	Dull, flat, grayish-white, dry	Oval, elongated; size, 7 to 9 by 2 to 2.5 microns	Fragile, branched	Buds frequently in whorl, at tips of mycelial segments; pellicle on broth

psilosis, and agglutinated well in the corresponding serum. Minor variations in morphology were observed. The strain depicted on the accompanying plate as M. parapsilosis (1) showed the morphology typical of the species. In the strain labeled M. parapsilosis (2) masses of buds developed about the ends of mycelial segments, resembling, though not to be mistaken for, the spherical clusters of larger spores formed by M. albicans. It is possible that there are differences of specific value between these strains, but they may be regarded provisionally as of one species.

M. Krusei.—One strain from the finger, one from the tongue and thirteen strains from the feces were typical examples of this species.

Unidentified Moniliae.—Six other strains, three of which were recovered from the skin and three from the feces, seemed to belong in the genus Monilia, but did not present the characteristics of any species known to us.

One strain (no. 1, table 2; no. 1, plate) produces a smooth, pasty, cream-colored colony on maltose or honey agar. It does not liquefy gelatin, but produces a short fuzz along the line of growth. Sediment forms in broth. Dextrose, levulose and saccharose are fermented with the production of acid and gas. Agglutination to practically the complete titer occurs in serums prepared against M. albicans, but there is no absorption of agglutinins.

Small budding forms, measuring 1.2 to 2.4 by 2.4 to 3.6 microns, are produced on honey and maltose agar. In cornmeal agar a fine

TABLE 2.—*Fermentation and Agglutination Reactions of the Six Unidentified Strains of Monilia Compared with Those of Four of Forty-Three Strains of M. Albicans, One of the Four Strains of M. Parapsilosis and One of the Fifteen Strains of M. Krusei Recovered in This Survey* *

	Fermentation					Agglutination					
	Dextrose	Levulose	d-Galactose	Maltose	Saccharose	M. Albicans	M. Candida	M. Parapsilosis	M. Krusei	Saccharomyces	Cryptococcus I
Titer of serums						1:500	1:500	1:1,000	1:500	1:200	1:500
M. albicans	A G	A G	A	A G	A	1:500	1:200	1:50	1:50	1:50	1:100
M. albicans	A G	A G	A G	A G	A	1:500	1:200	0	1:100	0	1:50
M. albicans	A G	A G	A	A G	A	1:500	1:200	1:20	1:200	1:20	1:200
M. albicans	A G	A G	A G	A G	A	1:500	1:500	1:50	1:100	1:50	1:500
M. parapsilosis	A G	0	A	A G	A	0	1:50	1:1,000	1:200	1:100	1:200
M. krusei	A G	0	0	A G	0	0	0	1:100	1:500	1:50	0
Unidentified moniliae											
1. From skin	A G	A	A	A G	A G	1:500	1:200	1:100	0	1:100	1:500
2. From feces	A	0	A	A	A	1:200	1:100	0	1:100	1:200	1:500
3. From skin	A G	0	A	A	0	0	0	0	0	1:200	0
4. From skin	A G	0	A	A	0	0	0	1:20	0	1:200	0
5. From feces	A G	0	A	A	0	0	0	0	1:50	1:200	1:100
6. From feces	A G	0	A	A	0	0	0	0	1:20	1:200	1:50

* A indicates acid; G, gas. All these strains gave negative results in raffinose, lactose, mannite, dextrin and inulin.

mycelium forms, and numerous small buds occur at the juncture of the cells. These buds increase to form irregular clusters, and sometimes become so numerous that a continuous sheath of buds surrounds the hyphal thread.

Two other strains (nos. 3 and 4, table 2; no. 3, plate) from skin seem identical, producing on honey and maltose agar a smooth, flat, grayish-tan colony. They do not liquefy gelatin, but produce a fine outgrowth along the line of the stab similar to that formed by the mycodermata. Also, like the mycodermata and M. krusei, they form a film in broth. Acid and gas are formed in dextrose; acid, in d-galactose, levulose and saccharose. The microscopic picture varies. On maltose and honey agar numerous budding forms are noted; these may

remain together in chains or in irregular groups. On cornmeal agar a fine branching mycelium is formed, which is fragile. The cells readily fall apart. Buds occur in long chains at the end of mycelial branches resembling chains of arthrospores. In ten-day cornmeal agar cultures the whole growth appears to be made up of chains of these elongated cells, each cell containing two or three fat globules. One is in some doubt whether to call these strains Moniliae. They seem to have many of the characteristics which Langeron [19] described for his new genus Geotrichoides. They do not agglutinate in serums prepared against M. albicans or the other species of Monilia studied, but show some cross-agglutination in a serum prepared against Saccharomyces.

Two of the unidentified strains from the intestinal tract (nos. 5 and 6, table 2) seem identical with these strains from the skin.

The only other unidentified strain of Monilia (no. 2, table 2; no. 2, plate) was obtained from the feces. It forms a smooth, cream-colored, pasty colony on honey and maltose agar, and produces a sediment in broth and a slightly nodular growth along the line of the stab in gelatin. There is no gas fermentation of sugars. Budding forms are produced on maltose and honey agar, and in cornmeal agar these budding cells form short chains resembling a mycelium. Agglutination occurs in a serum prepared against M. albicans, but there is no absorption of agglutinins. There is also some cross-agglutination in serums prepared against Saccharomyces and Cryptococcus, group I.

All of these unidentified strains proved nonpathogenic for rabbits. Intravenous injection of 1 cc. of 1:1,000 suspensions were without effect.

THE CRYPTOCOCCI

Most of the yeastlike organisms recovered from the skin or nails were cryptococci. These forms, being even simpler in their morphology than the moniliae, are more difficult to distinguish from one another. A detailed study of the morphologic, biochemical and serologic characteristics is being made with the hope that we may establish criteria by which individual species may be recognized. It has been possible, however, to differentiate four main groups on the basis of the colony characteristics:

Group I. Cryptococci forming smooth, pasty, white or cream-colored colonies.

Group II. Cryptococci forming rough, pasty, cream-colored or tan colonies. The colony is at first moist or cream-colored, but later becomes a deep tan with a dry and roughened surface.

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19. Langeron, M., and Talice, R. V.: Ann. de parasitol. **10**:1, 1932.

Group III. Cryptococci forming mucoid cream-colored or tan colonies. These cryptococci form a very moist, slimy, smooth growth, from a deep cream color to yellowish tan. The cultural picture is very like that of the pathogen, Cryptococcus hominis.

Group IV. Cryptococci forming pink colonies.

Cryptococci of the same types were found frequently in the alimentary tract.

THE MYCODERMATA

Next to the cryptococci, the organisms most frequently found on the skin or nails were mycodermata. These occurred usually on the toes, and all appeared to be of the same or closely related species (Mycoderma, group II, table 3). They form large tan, pasty colonies

TABLE 3.—*Yeastlike Organisms Recovered from One Hundred Normal Persons*

Organism	Source				
	Finger	Toenail	Toe Web	Tongue	Feces
M. albicans	0	0	0	6	18
M. parapsilosis	1	0	1	0	2
M. krusei	1	0	0	1	13
Monilia, unidentified	2	0	1	0	3
Cryptococcus, group I	28	32	23	5	12
Cryptococcus, group II	0	3	4	1	1
Cryptococcus, group III	2	2	1	1	3
Cryptococcus, group IV	19	2	4	0	10
Mycoderma, group I	0	0	0	0	41
Mycoderma, group II	4	23	8	0	0
Saccharomyces (species ?)	0	0	0	2	3
Zygosaccharomyces (species ?)	0	0	0	0	1

which are corrugated, without aerial mycelia. On cornmeal agar a mass of branching mycelium made up of long rectangular segments develops. At the ends of the hyphae the segments divide to form chains of elongated arthrospores. Budding may occur from the hyphal segments, and isolated cells with buds are scattered through the growth.

The fungus most frequently encountered in the intestinal tract was a mycoderma of a quite different type (Mycoderma, group I, table 3), forming a large, grayish-white, slightly downy colony and morphologically showing a coarse, branching mycelium with both intercalary and terminal chains of more or less rectangular, thick-walled arthrospores, apparently identical with Oidium lactis, a form frequently found in butter and milk.

RESULTS OF SURVEY

The number of strains of these various types obtained is shown in table 3. Yeastlike fungi were recovered from the skin or the nails of 72 per cent of the persons studied and from the alimentary tract of 80 per cent. In 38 persons two or more species were obtained from the skin

and nails, and in 29, two or more species from the alimentary tract. In 23 persons cryptococci were obtained from two areas of skin, and in 7 the strains so obtained appeared identical.

In one instance an unidentified monilia was obtained from the finger and one from feces of the same person, and it is probable that they were identical. In 10 persons cryptococci were obtained from both the skin and the intestines, and in five of these the strains from the two sources seemed to be of the same species.

PERSISTENCE OF MONILIA CARRIER STATE

It seemed of interest to determine whether the finding of M. albicans in the intestinal tract of normal persons was merely transitory and possibly due to the ingestion of some of these organisms. Cultures from 13 of the persons from whom this species was obtained were taken at intervals of one month for a period covering from one to six months. One case failed to show M. albicans on a second culture; another gave negative results on culture after four months; a third, after six months. The remaining 10 cases gave positive results for albicans on culture: 4 for six months, 2 for two months and the remaining 4 for one month.

In other cases we have obtained positive cultures from the same patient for periods of over a year, and it seems that, in some instances at least, there is a real colonization of some portion of the intestinal tract by this fungus.

CAUSE OF THE CARRIER STATE

In an effort to determine whether the reactions of intestinal contents favor its growth, determinations of the p_H of the stool specimens were made, with the following results:

Organism Recovered	p_H of Specimen
M. albicans	6.5 to 7.5
Cryptococci, group I	6.5 to 8.4
Cryptococci, group III	6.7 to 7.6
Cryptococci, group IV	6.7 to 7.5
Mycoderma, group I	6.3 to 8.4

The persistence of M. albicans in the intestinal tract apparently was not due to any peculiarity in the reaction of intestinal contents. The subjects were also asked whether they were in the habit of eating yeast. Fifteen said that they have taken yeast cakes occasionally, but these persons did not show any one type of yeastlike organism in the stools. None of the persons investigated gave a history of persistent diarrhea or other symptoms that could be attributed to Monilia infestation.

COMMENT

These findings agree with those of most observers, so far as they show that yeastlike organisms are frequently present on normal skin. However, when the species of these organisms was determined, it was found that a large majority of them were cryptococci and mycodermata. A few nonpathogenic species of Monilia were encountered, but M. albicans was never found. While this does not prove that M. albicans never occurs on normal skin, it is a sufficient indication that its presence is at least infrequent. The presence of distinct although related organisms on normal skin in no way diminishes the significance of finding M. albicans in cutaneous lesions. It has been shown in previous reports that this species occurs with great regularity in certain well-defined types of lesions of the skin and of the nails.[1] While its presence in these lesions and its absence in normal skin do not prove that it is the cause of the lesions in which it is found, these two facts make strongly suggestive evidence. At least, one may conclude that when one finds and identifies this species in a lesion of the skin, one is dealing with a definite group of dermatoses which, for the present, we may refer to as moniliasis.

In the gastro-intestinal tract the findings were different. Here, while a definite type of mycoderma and several species of Cryptococcus were the organisms most frequently recovered, M. albicans was found in 18 per cent of these normal persons and occurred persistently in a number of them. This in general agrees with the findings of Nye[11] and Ashford.[12] It indicates that this species may grow saprophytically in the intestinal tract without producing symptoms, and distinctly limits the significance of the finding of this organism in the feces in disease. At the same time, it should be recalled that in patients with moniliasis of the skin, M. albicans is present persistently in the intestines with considerable regularity.[1b] This suggests that the presence of the organism in the intestine may be the source of the infection in predisposed areas of skin, the cutaneous infection resulting in definite lesions.

SUMMARY

1. In a series of 100 normal young adults, M. albicans was not recovered from the skin or the nails.

2. Other yeastlike organisms, chiefly cryptococci and mycodermata, were obtained from the skin or nails in 72 per cent of this series.

3. Yeastlike organisms were obtained from the tongue or feces in 80 per cent of the cases studied.

4. These strains were again chiefly mycodermata and cryptococci, but M. albicans was recovered from the alimentary tract of 18 per cent of the persons studied.

MODIFICATION OF THERAPY WITH GOLD COMPOUNDS IN LUPUS ERYTHEMATOSUS

PRELIMINARY COMMUNICATION

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It is well established that the various gold chloride preparations may be given intravenously in cases of lupus erythematosus, sometimes with spectacular success. Though the results are often temporary, by persistence clinical "cures" are frequently obtained. However, one has only to pass an eye down the column headed "Gold" in the last few issues of the "Quarterly Cumulative Index Medicus" to realize the frequent occurrence of serious accidents following its use. The history of the therapeutic use of the various gold preparations in dermatology has roughly paralleled their use by the internists in pulmonary tuberculosis. At first hailed as a near-specific and later, because of their association with toxemic accidents and death, damned as a poison, they fell from their original high therapeutic position. Today the gold preparation is finding its level of efficiency as a drug of incomparable value in lupus erythematosus, of doubted value in the tuberculids and lupus vulgaris, and of much value in some stages of pulmonary tuberculosis (all of these statements being predicated on its careful and intelligent use, with due attention to its potentialities as a poison).

Efforts to avoid some of these unfortunate accidents have been made both by physicians and by the drug manufacturers. Instead of using gold sodium thiosulphate by vein, Monash and Traub [1] suggested its use intradermally in the diseased areas. This modification of therapy has apparently produced excellent results, and it eliminates the sudden suffusion of the circulating blood with a toxic substance, as occurs with intravenous injection, and therefore theoretically prevents the occurrence of much of the acute toxemic effect. These authors reported no untoward sequelae with the exception of a relatively mild tissue reaction and some pain, which was easily controlled by the addition of procaine hydrochloride to their solution. Manufacturers have attempted to reduce the toxicity of their product by a change in the chemical formula, but in most instances they have succeeded only in

1. Monash, S., and Traub, E. F.: Modification of Therapy with Gold Compounds in Lupus Erythematosus: Preliminary Communication, Arch. Dermat. & Syph. **24**:110 (July) 1931.

reducing its therapeutic efficiency. Recently, one concern has marketed gold sodium thiosulphate in a stable aqueous solution, instead of as a crystalline powder. This solution, ready for administration, eliminates the possible undesirable factor of contamination or the use of poorly distilled water in the preparation of the drug, and at the same time eliminates other possible chances of error. In a small clinic in which time and assistance are at a premium, such a preparation is of considerable value.

Monash and Traub [1] held that the beneficial effects of the gold preparations possibly depend on the concentration of the gold radical at the diseased site, and thus they explained much of the benefit derived from their therapeutic technic. However, Wigley [2] showed that after the intravenous use of gold chloride the diseased skin does not contain any demonstrable quantity of gold and, furthermore, that the skin of persons who have exfoliative dermatitis from the use of this drug does contain fairly high concentrations of gold. It would appear that one must find a more satisfactory explanation for its beneficial action in lupus erythematosus.

Following the communication of Monash and Traub, we began treatment in a case of lupus erythematosus, adhering to their technic except that we employed the prepared aqueous solution of gold sodium thiosulphate already referred to. Owing to the limited supply of this preparation we began to treat only a part of the diseased skin, i. e., one side of the face. After three weekly intradermal injections of 10 mg. each, improvement was manifest, but, strangely, the improvement occurred on the side of the face that had not been treated. The patient complained of the discomfort of multiple needle punctures, and recourse was had to a single subcutaneous injection in the upper part of the arm. Improvement progressed with the continuance of this manner of giving the drug, and the patient complained of little discomfort at the site of the injection. Dissemination of the report of the good results in this case among the Negro population brought four additional patients with lupus erythematosus for treatment. These patients have been similarly treated successfully, not more than 25 mg. of the drug being given at weekly intervals. A patient with a long-standing case of lupus vulgaris to whom much treatment had been given previously was also treated both intradermally and subcutaneously, with no apparent effect on the disease. Intramuscular injection of the gold preparation was attempted, but the patient complained of far more pain and discomfort than when it was given subcutaneously. All of these patients are under treatment at the present time, and all have presented immediate good results.

In spite of the small number of cases described, they serve to illustrate a modification of treatment with a relatively recent form of gold sodium thiosulphate which apparently will simplify the therapeutic approach to lupus erythematosus, as well as theoretically prevent severe reactions to gold. It is hoped that this communication may stimulate further reports.

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2. Wigley, J. E. W.: Some Observations on the Deposition of Gold in the Skin, Brit. J. Dermat. **44**:69 (Feb.) 1932.

PSEUDOXANTHOMA ELASTICUM AND ANGIOID STREAKS

A DISEASE SYNDROME WITH COMMENTS ON THE LITERATURE AND THE REPORT OF A CASE

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Pseudoxanthoma elasticum, known as an entity since Darier's communication [1] in 1896, was previously considered a variant of the true xanthomas. Before Darier's report, Rigal [2] and Balzer [3] observed degeneration of the elastic tissues, but they interpreted this finding as part of the xanthomatous process. Darier's classic description and pathologic study have since been corroborated and added to by many observers. Among the reports of this disease, Surmont's thesis [4] is probably the most complete. Throne and Goodman's study [5] included a review of the literature and a report of two cases; it is one of the best articles on pseudoxanthoma elasticum in the American literature.

Angioid streaks of the retina were first described by Pflange [6] in 1892. Some writers prefer to associate Doyne's name [7] with the initial characterization, since he reported a case in 1889 in which an injury to both eyes resulted in a picture resembling the condition. The term

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1. Darier, J.: Pseudoxanthoma elasticum, Monatsch. f. prakt. Dermat. **23**:609, 1896.

2. Rigal, D.: Observation pour servir à l'histoire de la chéloide diffuse xanthélasmique, Ann. de dermat. et syph. **2**:491, 1881.

3. Balzer, F.: Recherches sur les caractères anatomiques du xanthélasma, Arch. de physiol. **4**:65, 1884.

4. Surmont, J.: Contribution à l'étude du pseudo-xanthome élastique, Thèse de Paris, no. 392, 1925.

5. Throne, B., and Goodman, H.: Pseudoxanthoma Elasticum, Arch. Dermat. & Syph. **4**:419 (Oct.) 1921.

6. Pflange, O.: Pigment Striae with Secondary changes in the Retina after Hemorrhage, Arch. Ophth. **21**:282, 1892.

7. Doyne, R. W.: Choroidal and Retinal Changes, the Result of Blows on the Eyes, Tr. Ophth. Soc. U. Kingdom **9**:128, 1889.

"angioid" was introduced by Knapp [8] in 1892 as descriptive of the streaks. Up to the year 1931, sixty-five cases were reported in the American and foreign literature; and while the appearance is essentially the same in most instances, enough variation has occurred to indicate that not all of the reputed cases were those of true angioid streaks. This conclusion is strengthened by many of the illustrative drawings which show but little resemblance to the disease in question.

In 1929, Grönblad [9] and Strandberg [10] were the first to report striped formations in the subretinal area in three patients who also had pseudoxanthoma elasticum. They pointed out the possibility that the two conditions might have a common origin. Four similar cases were described by Marchesani and Wirz,[11] who told of a case of the two conditions combined demonstrated by Hallopeau and Lafitte [12] and of another reported by Welti.[13] One combined case was observed by Poos,[14] and two were reported by Krantz [15] and Hartung.[16] Clay [17] and Jones, Alden and Bishop [18] told of five cases in which the two diseases were found and of two instances in which angioid streaks and senile elastosis were present. Haack and Minder's [19] patient also showed the changes in the skin and the eyes. In a most comprehensive review of angioid streaks in combination with pseudoxanthoma elasti-

8. Knapp, H.: On the Formation of Dark Angioid Streaks as an Unusual Metamorphosis of Retinal Hemorrhage, Arch. Ophth. **27**:289, 1892.

9. Grönblad, E.: Angioid Streaks—Pseudoxanthoma Elasticum, Acta ophth. **7**:329, 1929.

10. Strandberg, J.: Verhandl. d. dermat. Gesellsch. Stockholm **13**:3, 1929.

11. Marchesani, O., and Wirz, F.: Die Pigmentstreifenerkrankung der Netzhaut, das Pseudoxanthoma elasticum der Haut; eine Systemerkrankung, Arch. f. Augenh. **104**:522, 1931.

12. Hallopeau and Lafitte: Nouvelle note sur un cas de pseudo-xanthome élastique, Ann. de dermat. et syph. **4**:595, 1903.

13. Welti, M. H.: Pseudoxanthoma elasticum (Darier) in Verbindung mit einer tuberkuloiden Granulationsbildung, Arch. f. Dermat. u. Syph. **163**:427, 1931.

14. Poos, J.: Ueber das gemeinschaftliche Auftreten von gefässähnlichen Netzhautstreifen und Pseudoxanthoma elasticum der Haut, Klin. Monatsbl. f. Augenh. **87**:734 (Dec.) 1931.

15. Krantz, W.: Pseudoxanthoma elasticum (Darier) und Pigmentstreifenerkrankung des Augenhintergrundes bei zwei Brüdern, Dermat. Wchnschr. **94**:233 (Feb. 13) 1932.

16. Hartung, H.: Ueber familiäre angioide Pigmentstreifenbildung des Augenhintergrundes, Klin. Monatsbl. f. Augenh. **88**:43 (Jan.) 1932.

17. Clay, G.: Angioid Streaks of the Retina and Pseudoxanthoma Elasticum, Arch. Ophth. **8**:334 (Sept.) 1932.

18. Jones, J. W.; Alden, H. S., and Bishop, E. L.: Pseudoxanthoma Elasticum, Arch. Dermat. & Syph. **27**:424 (March) 1933.

19. Haack, K., and Minder, E.: Zur Kasuistik des Pseudoxanthoma elasticum (Darier) mit Pigmentstreifenerkrankung des Augenhintergrundes, Arch. f. Dermat. u. Syph. **167**:717 (March) 1933.

cum, Grönblad [20] considered the syndrome to be one of disintegration of the elastic tissues, which is usually localized in the skin, the mucous membranes and the eyes, but which may also affect elastic tissue in other parts of the body, such as the walls of the blood vessels and the heart. The subject was further considered in another article by the same author.[21] It is of interest that since the communications of Grönblad [9] and Strandberg,[10] no true case of pseudoxanthoma elasticum has been reported as occurring alone and without the presence of angioid streaks. Clay reported two cases (already mentioned) in which angioid streaks were present and in which the skin showed senile elastosis. It is thus possible that in rare instances one or the other condition may be found alone, although the possibility of a mistaken diagnosis must be kept in mind. The number of combined cases reported to date is shown in the tabulation.

From the table, if one omits the case of pseudoxanthoma elasticum reported by Hallopeau and Lafitte and that reported by Welti

Number of Cases to Date in Which Angioid Streaks and Pseudoxanthoma Occur in Combination

Author	Angioid Streaks	Pseudoxanthoma Elasticum	Cases
Grönblad; Strandberg	+	+	3
Hallopeau and Lafitte	+ ?	+	1
Marchesani and Wirz	+	+	4
Welti	+ ?	+	1
Poos	+	+	1
Hartung, Krantz	+	+	2
Clay; Jones, Alden and Bishop	+	+	5
Haack and Minder	+	+	1

in which positive diagnoses of angioid streaks were not made, it is seen that sixteen cases have been reported in which both pseudoxanthoma elasticum and angioid streaks were demonstrated in the same patient. To this number we wish to add the case described in the following report:

REPORT OF CASE

Miss J. C., aged 26, an embroiderer, when seen on June 25, 1932, stated that she first noticed an eruption on her neck four years before. It appeared as small elevations, and she was certain that many of the lesions were pustules. During the year prior to presentation for treatment the pustular element was absent. A year following the appearance of the eruption on the neck, similar lesions were noticed in the region of the anterior borders of the axillae. Progressively, the antecubital fossae and the pubic and abdominal regions became affected, new outcrops appearing until six months prior to presentation. After that time no further

20. Grönblad, E.: "Angioid streaks"—Pseudoxanthoma Elasticum, Acta ophth. (supp. 1) **10**:1, 1932.

21. Grönblad, E.: Pseudoxanthoma Elasticum and Changes in the Eye, Acta dermat.-venereol. **13**:417 (Nov.) 1932.

involvement was noticed. There were no subjective symptoms, and the patient presented herself for cosmetic reasons, incident to the appearance of the eruption on her neck.

No history was obtained of familial consanguinity. The parents came from southern Italy. The father, aged 58, was alive and enjoyed good health. Her mother, who was always "sick and ailing" and who had poor eyesight, died when the patient was 2 months old. There were no full brothers or sisters, but there were one step-brother and four step-sisters, all of whom were in good health and did not have cutaneous or ophthalmic symptoms. A maternal aunt, aged 64, never had cutaneous manifestations, but her eyesight was diminished.

The patient had had chickenpox and measles when a child. The tonsils had been removed many years before. Six years before, the thyroid gland became enlarged, and she felt tired and nervous and lost weight. She consulted several

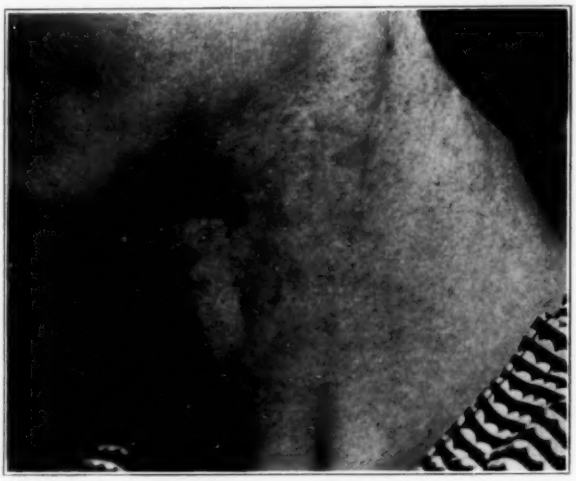

Fig. 1.—Patient with pseudoxanthoma elasticum, showing lesions on the left side of the neck.

physicians, and although a basal metabolism test was not made, she felt greatly improved as a result of taking the medicines prescribed.

Cutaneous Changes.—The cutaneous condition was seen to advantage on the front and sides of the neck. Here the skin was thrown into folds, the normal wrinkling of the skin being greatly exaggerated, giving the skin a loose, baggy appearance. On the surface of the skin were numerous smaller and larger, lemon-yellow elevations. Interspersed at irregular intervals were areas of apparent atrophy. There were also a few large comedo-like lesions and gaping mouths of follicles. When palpated, the affected skin had a peculiarly soft feel, likened by Darier to "damp velvet." The eruption was not well demarcated but gradually shaded into normal skin.

The disease was also present in both axillae, on the anterior borders of the axillae, over the epigastrium, and in the pubic region, the inguinal folds and the antecubital fossae. On these cutaneous areas the eruption was less pronounced than on the neck. The laxness of the skin was not so noticeable, and the individual

elevations were smaller. The lesions, however, were similar to the eruption on the neck. The scalp, face, back and legs were not affected.

The mucous membranes of the mouth and nose were also affected. In the mouth, the lesions were confined to the inner surface of the lower lip. Small, discrete papules were present and exhibited the same change in color as the cutaneous lesions.

Examination of the nose revealed yellowish ivory-colored papules in an area which involved about two thirds of the left side of the septum and a similar area on the lateral nasal wall. The picture was not unlike that of the mucous membrane of the lower lip. The mucous membrane of the right nostril was of normal color and appearance.

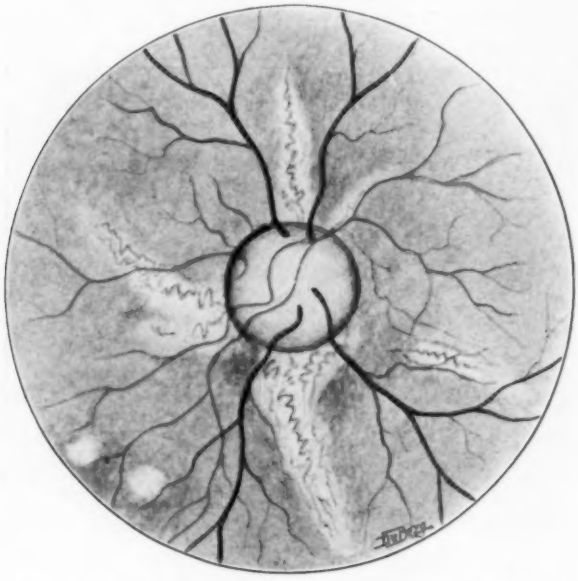

Fig. 2.—Angioid streaks in the fundus of the left eye.

Ocular Changes.—The external examination of the eyes showed nothing of importance. The vision in both eyes was 20/20 uncorrected. Examination of the disks revealed no abnormalities except at the margins. To the temporal side of the right disk and partially surrounding it, a dark brown zone was present. A similar zone was present to the nasal side of the left disk. The fundi were paler than normal. Radiating from the disks were numerous corkscrew-shaped lines which varied in color from pale red to black and which were surrounded by dirty gray, moth-eaten zones of varying widths. The color of the lines was not always the same throughout the entire length; at the origin of a line the color might be pale red, near the middle dark gray and at the termination pale red. These lines never passed the equator. They appeared to be subretinal, and there was no connection with the retinal vessels. One white, circumscribed patch covered with fine irregular vessels was present about two disk diameters above and to the nasal side of the left disk. One corkscrew-shaped line was also observed concentric with the disk in the left eye apart from the radiating ones. Two white patches about 1½ disk diameters below and to the temporal side of the disk were present in the

right fundus. Otherwise the fundi were normal. The fundi were studied with the hand battery and electric ophthalmoscopes, the binocular ophthalmoscope and the slit lamp.

Histology of the Cutaneous Lesion.—Skin was removed from the right side of the neck. This was studied by Dr. D. L. Satenstein, who reported as follows:

"Low Power Magnification: A change in both the physical and staining characteristics of the framework was noticed predominantly in the midcutis and less so in the deep cutis and subepidermic zone; it was fairly well marked about the

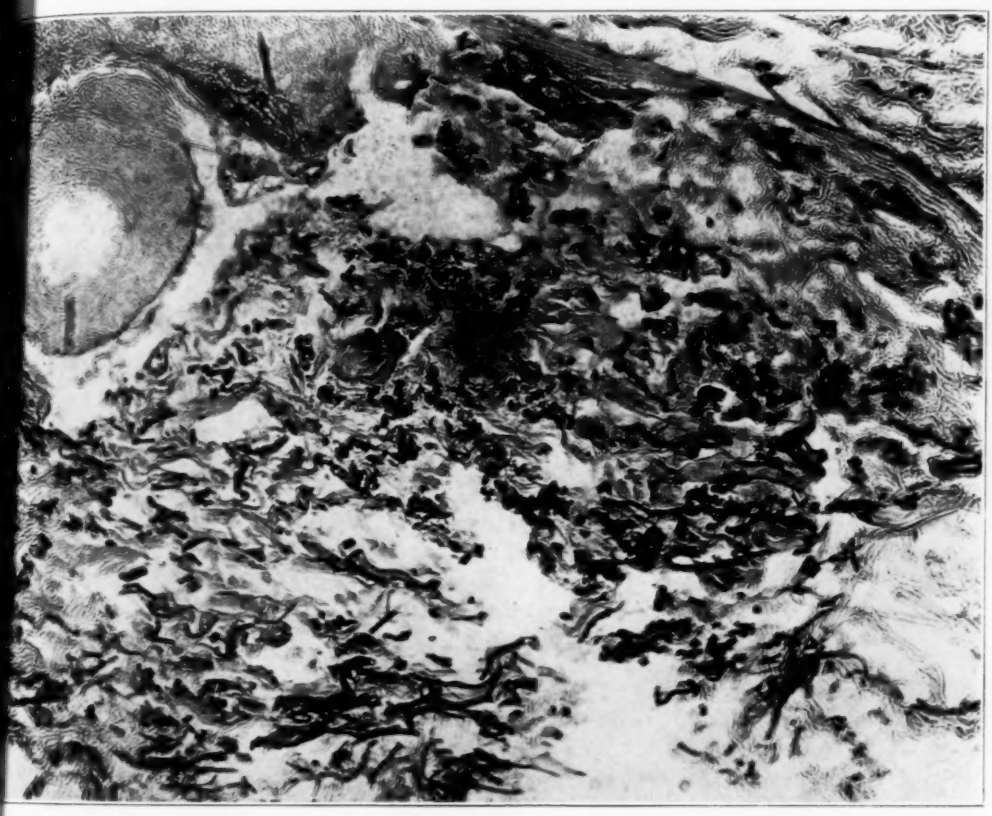

Fig. 3.—High power photomicrograph (reduced) of skin removed from the right side of the neck, showing disintegrated bundles of elastic tissue.

sebaceous glands but not at all in relation to the coil glands. In places the change was somewhat limited and in others fairly diffuse. In these zones the bundles of the framework of the cutis were fragmented and, in places, granulated. Aside from this, there was practically no other physical change. An occasional dilated blood vessel was noted. The stain of these fragmented and crumbled fibers was suggestive of light lilac or purple tones. Nowhere was there a tendency toward, or even suggestion of, a refraction of the affected parts. It was not possible with the routine hematoxylin-eosin stain to determine whether the pathologic fibers were collagen or elastic tissue. With Weigert's special elastic tissue stain (resorcin

fuchsin), counterstained with alcoholic orange G, the fragmented bundles were readily demonstrated to be elastic tissue, the collagen fibers being practically normal.

"High Power Magnification: The epidermis showed no appreciable change. There were a few lymphocytes about the papillary vessels. No giant cells were present. The sebaceous glands and hair follicles showed no variation from the normal, but some of the sweat glands showed a definite pathologic picture. The cells of the lining tubules were in a state of granular degeneration which had advanced to almost complete vacuolization, with marked shrinking of the nuclei."

Physical Examination.—A thorough physical examination revealed no abnormalities in the patient's heart, lungs, abdominal viscera or nervous system. There was an enlargement of the thyroid gland which was considered to be a colloid goiter. The basal metabolic rate was plus one. The Wassermann test was negative. A urinalysis revealed normal renal conditions. The blood pressure was 124 systolic and 80 diastolic. An examination of the blood showed that the hemoglobin was 80 per cent; the red blood cells, 4,200,000, and the white blood cells, 7,400. The blood chemistry was: uric acid, 1.9 mg., and urea nitrogen, 13.7 mg. per hundred cubic centimeters; sugar, 0.8 per cent; cholesterol, 0.156 per cent, and chlorides, 0.453 per cent.

Two of the patient's step-sisters were examined and found free from signs of cutaneous or ocular involvement. An unsuccessful attempt was made to get the patient's maternal aunt to report for examination.

Treatment.—While the patient was under observation, we instituted treatment with unfiltered roentgen rays in fractional dosage (90 roentgens) to the sides of the neck. Twelve treatments at weekly intervals were administered, constituting three erythema doses over approximately three months. Marked clinical improvement resulted, with diminution in the size of the lesions, a flattening of the surface of the skin and a return of the skin to a more normal color. No diminution in the folds or in the exaggerated lines of the skin, however, was noted. It was considered that the improvement resulted from the known degenerative effect of the roentgen rays on elastic tissue. If this is true, the pathologic process of fragmentation and degeneration of the elastic tissue in the skin was increased, thus terminating the process many months or years before cessation would ordinarily have taken place. The patient would not consent to the removal of a section of skin in the treated areas so that we might determine this point. It was suggested that the same effect might be obtained by instituting ultraviolet ray therapy in erythema doses. The congestion thus produced should theoretically aid absorption of the degenerative elastic tissue.

COMMENT

Pseudoxanthoma Elasticum.—Pseudoxanthoma elasticum, although a rare disease, offers distinctive characteristics sufficient for a clinical diagnosis. These characteristics have been described in the report of our case and need not be repeated. Friedmann [22] differentiated between typical or true and atypical or false cases. The true cases bore out Darier's descriptions, whereas the false were like Darier's cases in some particulars but differed in many essential points. In the latter group are found diseases such as colloid milium, naevus elasticus, amyloid

22. Friedmann, M.: Ein Beitrag zur Kenntnis des Pseudoxanthoma elasticum (Darier), Arch. f. Dermat. u. Syph. **134**:151, 1921.

degeneration and senile degeneration of elastic tissue. Mixed cases have also been reported in which it has been difficult to arrive at an accurate clinical or pathologic diagnosis.

The histologic evidences of pseudoxanthoma elasticum are fragmentation and degeneration of the elastic tissue, particularly in the mid-cutis and the deep cutis, without an accompanying destruction of collagen fibers. Other findings, such as the presence of giant cells, calcification, infiltrates and changes in the blood vessels, have been noted in a few instances. In our patient, some of the coil glands showed advanced degeneration in the cells of the lining tubules. The striking feature in all cases, however, is the primary involvement of elastic tissue. Kissmeyer and With [23] and Weidman [24] have pointed out the close resemblance, pathologically, between pseudoxanthoma elasticum and certain instances of elastosis senilis. After a study of specimens from fifteen senile skins, Weidman [24] stated that "pseudoxanthoma elasticum is almost identical with some senile elastoses" and concluded that "histologic observations per se do not form an adequate basis for a differential diagnosis between pseudoxanthoma elasticum and senile elastosis." Jones, Alden and Bishop [18] go further and aver that "histologically the two conditions cannot be differentiated." Montgomery [25] stated that "by the use of Unna's differential stains . . . the typical case of pseudoxanthoma elasticum can readily be distinguished, histologically, from so-called senile elastosis or senile changes in the skin." He based this conclusion on the presence of histopathologic changes in the collagen fibers in the latter condition and on the absence of such changes in pseudoxanthoma elasticum.

The cause of pseudoxanthoma elasticum is unknown. Evidence has accumulated which indicates that heredity plays a large part, and Michael [26] stated that the disorder is probably "inherited as a recessive condition." Jones, Alden and Bishop [18] entertained the belief that since the disease is allied to the changes found in elastosis senilis, it is an evidence of presenility.

Angioid Streaks.—Angioid streaks exhibit a definite clinical picture, and certain essential criteria must be present in order to establish a diagnosis of this disease. Brown zones about the margins of the disks are occasionally seen in apparently normal eyes, so that their presence, while almost constant, is not pathognomonic of angioid streaks. Since

23. Kissmeyer, A., and With, C.: Histological Studies of the Pathological Changes in the Elastic Tissues in the Skin, Brit. J. Dermat. **34**:175 (June) 1922.

24. Weidman, F. D.: The Pathology of the Yellowing Dermatoses, Arch. Dermat. & Syph. **24**:954 (Dec.) 1931.

25. Montgomery, H., in discussion on Jones, J. W.; Alden, H. S., and Bishop, E. L.: Pseudoxanthoma Elasticum, Arch. Dermat. & Syph. **27**:438 (March) 1933.

26. Michael, J. C., in discussion on Jones.[25]

the disease has a tendency to be chronically progressive, the ocular findings change from one time to another. The color of the streaks may thus at different times vary from pale red to gray, brown or black. This was illustrated in the case reported by Coppez and Danis.[27] After years hemorrhages may occur, changes in the connective tissues may take place, and if the region of the macula is sufficiently involved, vision becomes impaired.

Angioid streaks resemble retinitis striata, disease of the vascular system and pigmentary stripes following certain types of insult to the retina and choroid. In the latter conditions, the lesion may occur in any part of the retina, only one eye may be affected, the lesions are not necessarily progressive, and the characteristic peripapillary ring is absent.

The pathology of angioid streaks has not yet been determined. Verhoeff's report [28] is open to criticism because in his case a clinical diagnosis had not been made. Friedenwald [29] was unable to find a pathologic explanation for the ophthalmoscopic picture of angioid streaks. His patient had a cutaneous disorder not definitely diagnosed. At autopsy a widespread amyloid disease was noted. The eyes had been sectioned before this discovery, so that it was impossible to stain the ocular tissues for amyloid.

Various theories which pertain to the etiology of angioid streaks and to the mechanics of the lesions of the fundi have been promulgated, but none has been completely convincing. The more important of these are the following:

1. The condition is due to a constitutional congenital predisposition (Poos [14]).

2. It is a congenital abnormal development (Pretori [30]).

3. Displacement of the pigment epithelium produces folding formations in the inner membranes of the eye (Guist [31] and Walser [32]).

4. The ocular findings are due to a tearing of the layer of pigment epithelium of the retina (Doyne [7]).

5. The streaks are due to a cicatricial contraction of the fibrous tissue which replaces the deeper layers of the choroid (Verhoeff [28]).

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27. Coppez, H., and Danis, M.: Sur les stries angioides de la retiné, Arch. d'opht. **42**:649, 1925.

28. Verhoeff, F. H.: Nature and Pathogenesis of Angioid Streaks in Ocular Fundus, Tr. Sect. Ophth., A. M. A. 1928, p. 243.

29. Friedenwald, J.: Personal communication.

30. Pretori, H.: Ein Fall von eigenthümlicher Pigmentierung des Augenhintergrundes, Beitr. z. Augenh. **24**:101, 1898.

31. Guist, N.: Ein Fall von Pigmentstreifen der Netzhaut, Klin. Monatsbl. f. Augenh. **64**:565, 1920.

32. Walser, B.: Three Cases of Peculiar Pigmented Striations in the Fundus, Arch. Ophth. **25**:365, 1896.

6. The picture results from a thrombosis of the short posterior ciliary veins which pass through the sclera in an anomalous manner (Clay [17]).

7. The condition results from the proliferation of new vessels into scar tissue (Lister [33]).

8. Retinal hemorrhages are responsible for the condition (Pflange,[6] Knapp,[8] de Schweinitz [34] and Holden [35]).

9. Angioid streaks are pigmented vessels of inflammatory or congenital origin (Zentmayer [36]).

10. The streaks are in reality branches of the posterior ciliary arteries. The pigmented appearance is due to the deposition of insoluble blood pigment in the perivascular spaces (Collins [37]).

11. The appearance is due to tears in the coat of the choroid or in the glass membrane, due to the disappearance of the elasticity of the membrane following some degenerative process. They are thus optical phenomena similar to a break in glass (Kofler [38]).

This last explanation is in our opinion the most logical. We believe that the corkscrew-shaped lines (angioid streaks) appear as the result of a contraction of the elastic lamina of the choroid, which produces a tearing or break in this membrane. If the break is over a choroidal vessel, the color of the vessel is reflected through the break and is seen as a reddish streak. If the break is over the intervening choroidal tissue, the streaks assume a darker hue, from dark gray to black. If these deductions are correct, the cause of the pathologic change in the eye and the skin may be the same, and, if so, would point to a disease syndrome combining pseudoxanthoma elasticum and angioid streaks.

SUMMARY

1. In a careful review of the literature, we found that in sixteen reported cases diagnoses were made of pseudoxanthoma elasticum and angioid streaks in the same patient.

2. In the patient described in this paper, the lesions of the skin and mucous membranes simulated those described originally by Darier as

33. Lister, W. T.: Angioid Streaks of the Retina, Ophth. Rev. **22**:150 (June) 1903.

34. de Schweinitz, G. E.: Diseases of the Eye, ed. 10, Philadelphia, W. B. Saunders Company, 1924, p. 522.

35. Holden, W. A.: On the Probable Hemorrhagic Origin of the Striated Affections of the Retina, Arch. Ophth. **24**:147, 1895.

36. Zentmayer, W.: Angioid Streaks in the Retina with the Report of a Case, Tr. Am. Ophth. Soc. **12**:267, 1909.

37. Collins, E. T.: On the Etiology of Angioid Streaks in the Fundus Oculi, Tr. Ophth. Soc. U. Kingdom **43**:273, 1923.

38. Kofler, A.: Beiträge zur Kenntnis der Pigmentstreifenerkrankung, Arch. f. Augenh. **82**:134, 1917.

to distribution and morphology. Lesions were also found in the nasal mucosa. The pathologic picture confirmed the clinical diagnosis of pseudoxanthoma elasticum and also showed degeneration in the coil glands. There were no changes in the sebaceous glands or the hair follicles, and no giant cells were present. Treatment to the neck by means of roentgen rays resulted in apparent improvement in that area, this change being considered due to the destructive nature of the rays increasing the process of degeneration and absorption of the fragmented elastic tissue.

3. The changes in the eyegrounds were similar to those described in all of the authentic combined cases. The changes were probably of the same nature as those in the skin and depended for the clinical appearance on the tearing or breaking of the elastic lamina of the choroid. The site of the disturbance is thus in the subretinal area.

4. We believe with Grönblad [20] that a new disease syndrome is established in which elastic tissue is the site of the disturbance; it is usually seen in the skin, the mucous membranes and the eyes, but it may also affect elastic tissue elsewhere, as in the blood vessels and in the heart. The cause of the condition is unknown, but we believe that a hereditary predisposition is present.

5. While it is unwise to add to medical nomenclature without good reason, neither angioid streaks nor pseudoxanthoma elasticum is a suitable name for the combined disease. We suggest that the term elastosis atrophicans be used to designate the disease syndrome described in this paper.

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ROENTGEN TREATMENT OF THE PRIMARY LESION OF TULAREMIA

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Desjardins [1] and others showed that x-rays are of particular value in the treatment of boils, carbuncles and cellulitis in the infiltrative stage. These rays have no bactericidal effect. Their value is based on the fact that the infiltrating cells are destroyed by the action of x-rays. Whatever protective substance the infiltrating cells have is liberated more rapidly and made available for defensive purposes. Small doses of x-rays are used in preference to large doses. This destruction of cells by the small dose, if it has not favorably altered the course of the condition, has not done any harm.

Desjardins mentioned a case of anthrax in which roentgen treatment was given by Tillier.

I wish to report two cases of acute tularemia in which one exposure was made to one-half unit erythema dose of unfiltered x-rays.

REPORT OF CASES

CASE 1.—H. S., aged 25, a meat-handler, presented himself on Oct. 22, 1932, with a throbbing, painful, swollen, erythematous thumb with marked lymphangitis extending up to the axilla. The temperature was 100 F., and the pulse rate was 120. Slight headache and pains in the joints were present. The patient gave a history of cleaning rabbits (shipped in from Kansas) three days previously. He did not recall pricking his thumb. On close examination of the thumb for the point of entrance of infection, a small brownish area could be discerned. Otherwise the lesion appeared like an area of cellulitis which had a foreign body embedded in its center, but a roentgenogram failed to show the presence of the latter.

The patient was given one-half unit erythema dose of unfiltered x-rays over the affected area. Hot wet dressings of boric acid were applied to the thumb and arm. It was my intention to incise the lesion as soon as the area presented fluctuation. On the following day the patient reported that the pain, which affected the thumb and extended up the arm, had ceased three hours after he had received the roentgen treatment. The redness and swelling of the thumb, together with the lymphangitis and tenderness, had disappeared. The temperature and pulse rate became normal. There was no axillary tenderness. The patient made an uneventful recovery.

On the first day of examination the agglutination test for tularemia was negative. The agglutination test taken on November 3 (about thirteen days after the inoculation) gave a reading of 1:320. On Jan. 9, 1933, the agglutination test was positive, 1:80.

From the Pittsburgh Skin and Cancer Foundation.

1. Desjardins, A. U.: Radiotherapy for Inflammatory Conditions, J. A. M. A. **96**:401 (Feb. 7) 1931.

CASE 2.—A. R., a butcher, aged 19, presented himself on Nov. 29, 1932, with a history of having pricked the middle finger of the left hand with a knife while he was cleaning rabbits. He recalled distinctly that it was on November 26 that this accident occurred. Having worked in the same market with the previous patient, he was "tularemia conscious."[2] He applied mercurochrome to the lesion, and only when he had noticed that he felt "grippy" did he become suspicious that he might have "rabbit fever." On examination there was a small brownish area the size of a pinpoint under the nail, with redness and slight swelling of the tip of the finger. He complained of pain in the palm, and there was slight redness discernible. The temperature was 100 F. and the pulse rate, 110. There was no lymphangitis, but there was some tenderness in the axilla. One-half unit erythema dose of unfiltered x-rays was applied over the lesion. The patient stated that the following day, six hours after treatment, the pain in his finger subsided. The temperature and pulse rate became normal. He made an uneventful recovery.

An agglutination test for tularemia on November 29 was negative. On December 6 (fourteen days after inoculation), the reading was positive, 1:160. On Jan. 17, 1933, the reading was positive, 1:80.

PATHOLOGY OF THE PRIMARY LESION

Francis[3] stated that the primary lesion of tularemia shows a diffuse necrosis with nuclear fragmentation, and that the infiltration is mostly of polymorphonuclear leukocytes.

Downs[4] showed experimentally with rabbits that the primary lesion of tularemia consisted of a somewhat reddened area about 2 cm. in diameter, and that induration developed in from forty-eight to seventy-two hours. Microscopically, the epithelium showed little damage, but the subcutaneous tissue showed streaks of infiltration with fragmentation of the polymorphonuclear leukocytes. There was some proliferation of vascular endothelium, with many mononuclears surrounding the blood vessels in the deeper tissues.

PERIOD OF INVASION

Downs[4] further demonstrated that in normal animals the organisms invaded the blood stream quite regularly on the third or fourth day after infection, and that the organisms remained in the blood stream until death.

The average period of incubation in 259 cases reported by Francis[3] was three and a half days.

In the two cases reported here, I am reasonably sure that the patients were given roentgen treatment prior to the fourth day of the illness. If

2. Blackford, S. D.: Tularemia in Differential Diagnosis: Review of Thirteen Cases, Virginia M. Monthly **58**:10 (April) 1931.

3. Francis, Edward: Symptoms, Diagnosis and Pathology of Tularemia, J. A. M. A. **91**:1155 (Oct. 20) 1928.

4. Downs, Cornelia M.: Immunologic Studies on Tularemia in Rabbits, Infect. Dis. **51**:191 (Sept.-Oct.) 1932.

the average period of incubation of tularemia is three and a half days, I believe that the roentgen treatment arrested the progress of disease in these two cases. The treatment more than likely attenuated the bacteria located in the original focus. In addition thereto, it may have supplied some increased phagocytic power to the circulating lymphocytes.[1]

I have applied roentgen treatment to the axillary glands themselves prior to suppuration in other cases, but this did not prevent suppuration nor did it have any material effect on the progress of the disease.

CONCLUSION

These two cases, although not conclusive, are at least suggestive of the value of x-ray, in small doses in early infection with the B. tularense, prior to the fourth day after inoculation.

Early diagnosis is of distinct value for this type of treatment. Both the physician and those persons who clean rabbits should become "tularemia conscious" with the appearance of an infected area and the development of a vague fever.

SUMMARY

1. Two primary lesions of tularemia were treated on or about the third day with a dose of a half unit of unfiltered x-rays.

2. The evidence presented is suggestive that the progress of the disease was arrested.

EPIDERMOPHYTIDS AND THE TRICHOPHYTIN REACTION

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WITH DISCUSSION BY CHARLES MALLORY WILLIAMS, M.D.

How shall one designate the vesicular or squamous eruptions of the hands which accompany fungous infections of the feet? How is one to decide, in these cases, whether the eruption on the hands is caused by the fungous infection, by some external irritant or by some internal toxic condition? These questions are of great practical importance and confront the dermatologist in his contact with the many cases of this nature. We do not, of course, include in our consideration those cases of fungous infection of the feet which are accompanied by an eruption on the hands to which a definite cause can be assigned by the objective appearance, the history or patch tests. We are interested in the cases in which the explanation for the lesions on the hands is not quite so obvious and in which the only tangible evidence is the finding of fungi in the lesions of the feet and the absence of fungi in the lesions of the hands.

Williams and Bloch have done much for the development of the concept of the "id" in the cases of superficial mycotic infections of the skin. The work of W. Jadassohn and Peck [1] was most comprehensive and thorough in showing that the "vesicular and squamous changes on the hands, which accompany so many of the cases of epidermophytosis of the feet, are epidermophytids secondary to the hematogenous transport of living fungi from the primary lesions of the feet." This work is so generally known that it would be repetitious to cite the details of the investigations.

Suffice it to say that the diagnosis of epidermophytids of the hands is based on three criteria: (1) the finding of fungi in the lesions on the feet, (2) the absence of fungi in the lesions on the hands and (3) a positive reaction to the intradermal injection of trichophytin.

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1. Jadassohn, W., and Peck, S. M.: Arch. f. Dermat. u. Syph. **158**:16, 1929. Peck, S. M.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:40 (July) 1930.

If we are to accept these criteria, we must believe that fungi are not found in the so-called "id" lesions and we must not doubt the specificity of trichophytin.

Our work was originally contemplated, not with a preconceived skeptical attitude, but rather with the idea of enlarging the concept. We assumed the truth of the concept and hoped to find some relationship between the reactions to trichophytin in high dilutions and active

Data on Thirty-Eight Cases

Case	Lesions of Feet: Symptomatic	Lesions of Feet: Asymptomatic	Lesions of Hands: Symptomatic	Lesions of Hands: Asymptomatic	Examination of: Feet for Fungi	Examination of: Hands for Fungi	Results of Trichophytin Tests: 1:20	1:100	1:500	1:1,000	1:3,000	1:5,000
1. L. A.	0	0	+	0	0	0	++++	0	0	0	0	0
2. M.	+	0	0	0	0	—	++++	+++	+++	+++	±	±
3. M. A.	+	0	0	0	Monilia	—	+++	+	+	0	0	0
4. A. I.	0	+	+	0	0	0	0	0	0	0	0	0
5. M. S.	0	+	+	0	0	0	0	0	0	0	0	0
6. L. S.	0	0	+	0	0	0	+++	0	0	0	0	0
7. B. M.	0	+	+	0	+	0	0	0	0	0	0	0
8. L. S.	0	0	+	0	0	0	++++	+++	0	0	0	0
9. S. B.	0	+	+	0	+	0	++++	+++	+++	+++	+++	+++
10. H. F.	0	+	+	0	0	0	+++	++	+	0	0	0
11. L. N.	0	+	+	0	0	Monilia	++++	++	0	0	0	0
12. R. A.	0	+	+	0	0	0	+	0	0	0	0	0
13. M. F.	0	0	+	0	—	0	0	0	0	0	0	0
14. L. S.	0	+	+	0	+	0	0	0	0	0	0	0
15. V. C.	0	+	+	0	0	0	++++	0	0	0	0	0
16. E. R.	0	+	+	0	0	+	++++	+++	0	0	0	0
17. A. M.	0	+	+	0	0	0	0	0	0	0	0	0
18. H. L.	0	0	+	0	0	0	0	0	0	0	0	0
19. M. J.	+	0	+	0	0	0	++++	+++	+	0	0	0
20. C. B.	0	+	+	0	+	0	++++	+++	++	0	0	0
21. D. B.	0	+	+	0	Monilia	0	0	0	0	0	0	0
22. R. V.	+	0	+	0	+	0	0	0	0	0	0	0
23. I. F.	0	+	+	0	Monilia	0	++++	+++	++	+	+	0
24. J. K.	+	0	+	0	+	0	++++	++	++	+	±	0
25. P. D.	+	0	0	0	0	—	++	+++	++	0	0	0
26. H. T.	+	0	+	0	0	0	±	±	0	0	0	0
27. R. G.	+	0	+	0	+ and monilia	+ (nail)	0	0	0	0	0	0
28. D. P.	+	0	0	0	+	0	++	+	0	0	0	0
29. F. D.	0	+	+	0	+	0	+++	++	+	0	0	0
30. H. Z.	+	0	0	0	+	—	0	0	0	0	0	0
31. C. B.	0	+	+	0	0	0	++++	++	++	++	0	0
32. K. C.	0	+	+	0	0	0	+	+	±	0	0	0
33. J. F.	0	+	+	0	Monilia	0	+++	++	0	0	0	0
34. L. K.	+	0	+	0	+	0	0	0	+ (?)*	0	0	0
35. F. P.	+	0	+	0	0	0	0	0	0	0	0	0
36. S. B.	0	+	+	0	0	0	++++	++	+	+	+	±
37. M. R.	+	0	0	0	+	—	0	0	0	0	0	0
38. J. L.	+	0	+	0	+	0	0	—	—	—	—	—

fungous infections. We thought that possibly those patients who had had epidermophytosis, or those who had only quiescent foci of infection, would not react or would not react as strongly to the higher dilutions of trichophytin. We assumed the specificity of trichophytin. However, we obtained results which cast doubt on some of the aspects of the theory of epidermophytids and on the specificity of trichophytin.

We examined thirty-eight patients with a clinical diagnosis of epidermophytosis of the feet, of the hands or of both, made in the routine examination in the dermatologic clinic of the Stuyvesant Square Hospital. We made microscopic and cultural studies of the lesions, and

we injected trichophytin intradermally in the following dilutions: 1:20, 1:100, 1:500, 1:1,000, 1:3,000 and 1:5,000. The trichophytin employed was a commercial product. In some cases we checked the reactions with trichophytin prepared in our laboratories, finding no discrepancies.

The observations that we made are clearly set forth in the accompanying table. Examination of the table reveals the following facts:

1. There was, apparently, no relation between the severity of the infection and the response to injections of trichophytin.

2. Of the thirty-eight patients whose condition was diagnosed clinically as epidermophytosis, twenty-three showed a positive reaction to trichophytin.

3. Only Monilia could be recovered from the lesions of five patients, and four of these showed positive reactions to trichophytin.

4. Eight patients had demonstrable fungi in the lesions on the feet and negative responses to trichophytin. Seven of these patients presented accompanying vesicular or squamous lesions of the hands, not inconsistent with the accepted picture of palmar and digital epidermophytid.

5. Though a patient may give negative reactions to repeated injections of trichophytin if different sites are selected, a positive reaction will frequently occur if the site of a previous injection is selected (case 34).

COMMENT

In diagnosing epidermophytosis and epidermophytids it is not clear whether emphasis is to be laid on the laboratory findings or on clinical observations. In a recent publication Scholtz [2] stated that he could not accept the conception of palmar and digital epidermophytids without further clinical elucidation.

All of our patients presented a condition diagnosed clinically as epidermophytosis, and yet only twenty-three, or 60.5 per cent, gave a positive reaction to trichophytin. If we agree that the trichophytin test is specific, we must deduce from these findings either that in fifteen, or 39.5 per cent, of our patients the condition was diagnosed incorrectly, or that not all persons showing local fungous infection present systemic disease or allergy.

The problem thus stated would be simple were it not for two additional disturbing features: First, our original premise, that trichophytin is specific, is subject to doubt. As Scholtz [2] pointed out, its specificity is disputed by many, including J. Jadassohn,[3] Arnold,[4]

2. Scholtz, M.: Epidermophytids as a Clinical Conception, Arch. Dermat. & Syph. **25**:812 (May) 1932.

3. Jadassohn, J.: The Importance of Immune Biologic Processes in the Morphology of Skin Lesions, Arch. Dermat. & Syph. **21**:355 (March) 1930.

4. Arnold: Arch. f. Dermat. u. Syph. **136**:225, 1923.

Sloimovici and Ullmo [5] and Darier. In four of the five patients in our series from whose lesions only Monilia could be recovered, there were positive reactions to trichophytin. Ravaut,[6] too, reported that he found positive reactions in persons with lesions caused by the yeast cells. These findings hardly speak for the specificity of the test. It follows logically that in attempting to differentiate fungous from nonfungous diseases it is not incorrect to hesitate about placing absolute reliance on trichophytin as a diagnostic aid.

It may be argued, however, that the so-called false positive reactions indicate that the patient had had epidermomycosis and that the allergy had persisted. This position was taken by Bloch. To answer this brings us to our second and more important point. We found eight cases in which fungi were demonstrable in the lesions on the feet and in which the trichophytin test was negative. In seven of these cases, vesicular and squamous lesions on the hands, consistent with the accepted picture of epidermophytids, accompanied the fungous infection of the feet. Williams and Carpenter,[7] in a study of seventy cases, found five in which fungi were recovered and in which the trichophytin test was negative. Pels and Schlenger [8] found ten instances of clinical epidermophytosis with demonstrable fungi in which the trichophytin test was negative.

Our seven cases satisfied the clinical criteria for a diagnosis of epidermophytosis with epidermophytids. The appearance of the hands and feet, the obviously active lesions, the duration varying from two weeks to two years, the presence of fungi in the feet and the absence of fungi from the hands certainly point to such a diagnosis. In daily routine dermatologic examinations this diagnosis is made in such cases without hesitation. Yet in these seven cases, the important criterion, a positive trichophytin test, was missing! Even were we not to dispute the reliability of this test, and were we to assume its specificity, these seven cases were perfect examples of conditions in which one would expect a positive reaction to trichophytin. According to the generally accepted formulas, the lesions on the hands were epidermophytids and as such were local manifestations of a systemic disease brought on by the hematogenic transport of fungi from the lesions on the feet.

It is obviously difficult at this point to classify these cases properly and logically. If the trichophytin test is specific, the lesions in seven of our cases were not epidermophytids and belonged in another category, because an allergic state is indicated by a positive reaction to tricho-

5. Sloimovici, M. A., and Ullmo, A.: Ann. de dermat. et syph. **8**:554, 1927.

6. Ravaut: Presse méd. **36**:1443 (Nov. 14) 1928.

7. Williams, C. M., and Carpenter, C. C.: Trichophytin in Diagnosis, Arch. Dermat. & Syph. **25**:847 (May) 1932.

8. Pels and Schlenger: South. M. J. **25**:1066 (Oct.) 1932.

phytin. This would make evident the fact that other conditions, such as eczema, can be perfect replicas of epidermophytids. It would also make evident the fact that in cases of vesicular and squamous eruptions on the hands or on the body, the mere presence of tinea pedis does not necessarily indicate any correlation between the conditions. If, on the other hand, the trichophytin test is not specific, and this is not too unreasonable to believe, there is no specific means of distinguishing between eczema, dyshidrosis and epidermophytid.

Only one explanation can be offered for the negative reaction to trichophytin in patients who seem clinically to present typical epidermophytids. That is that these negative responses represent a state of anergy. It seems to us that this is pure assumption based on the presupposition that the lesions in all such patients are epidermophytids, despite the negative trichophytin reaction.

It is true that in the exhaustive stages of tuberculosis, and also in lupus miliaris disseminatus, the tuberculin test can be negative and still not rule out tuberculosis. This is based, however, on the known fact that tuberculosis is a systemic disease. This is not absolutely conceded for superficial epidermomycosis. The isolated instances in which fungi were found in the blood stream in human beings by Peck, Strickler, Ozellers and Zaletel,[9] and a few others have been so rare that we can hardly generalize and assume that in all cases of tinea pedis accompanied by vesicular or squamous lesions elsewhere the latter represent a reaction to living fungi which have been carried through the blood stream. The most we can concede, at this time, is that in the rare cases in which fungi were recovered from blood cultures, the pathogenicity was proved.

Lupus erythematosus is not uncommonly found in patients suffering from tuberculosis. The close association, statistically, has been recorded by Boeck,[10] Roth,[11] Sequeira and Balean [12] and many others. Tuberculosis has been produced in animals inoculated with material from cases of lupus erythematosus by Gougerot,[13] Ehrmann,[13] Reines and Block [13] and Fuchs.[13] On the other hand, lupus erythematosus has followed dermatitis seborrhoeica, acne, variola, erysipelas, chemical irritation and overexposure to sunlight. It has, too, been found associated with nonrheumatic verrucous endocarditis and nephritis.[14] The most

9. Strickler, A.; Ozellers, E. A., and Zaletel, R. P.: Modern Interpretation of Mycotic Infections of the Feet and Hands, Arch. Dermat. & Syph. **25**:1028 (June) 1932.

10. Boeck: Arch. f. Dermat. u. Syph. **42**:71, 1898.

11. Roth: Arch. f. Dermat. u. Syph. **51**:3, 1900.

12. Sequeira and Balean: Brit. J. Dermat. **14**:367, 1902.

13. Cited by Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 766.

14. Libman and Sacks: Tr. A. Am. Physicians **38**:46, 1923.

that we can say, then, is that in some instances lupus erythematosus is of tuberculous etiology. This analogy is not inappropriate, we believe, in showing the error of universal deductions from comparatively few specific instances.

The lesions on the hands accompanying fungous infections of the feet may be local infections of ectogenous origin. Though it is true that many observers point to the usual absence of fungi in the hands we cannot peremptorily discard the reports, referred to by Scholtz, of Sicoli,[15] Ormsby and Mitchell,[16] C. J. White and Darier, who found demonstrable fungi in a fairly high percentage of the lesions on the hands. Mitchell [17] stated, in 1929, that he saw no reason for assuming that because there is a mycotic infection of the feet a coexisting dermatosis of the hands must be mycotic. He asserted that he did not find it more difficult to demonstrate the fungus in the hands than in the feet in cases in which the condition seemed to be mycotic. The fact that in many cases the eruption on the hands persists for a long time after the lesions on the feet have been cleared up also militates against the theory that vesicular and squamous eruptions on the hands accompanying tinea pedis are necessarily "ids."

We have frequently encountered patients with tinea pedis and with positive trichophytin reactions who presented vesicular and squamous lesions on the hands, and questioning and examination elicited the information that occupational irritants were the etiologic agents. These eruptions on the hands not infrequently were clinically indistinguishable from squamous or vesicular epidermophytids.

SUMMARY

1. The work of Bloch, Williams, W. Jadassohn and Peck and others points to the fact that in many cases superficial mycotic infections of the feet can give rise to epidermophytids on the hands and on other parts of the body.

2. The apparently simple explanation of the eruptions on the hands which often accompany tinea pedis has given rise to an unwarranted abuse of this conception. We believe that the diagnosis of epidermophytid of the hands has been made in innumerable cases in which there was no basis for such an assumption.

3. We encountered seven cases which were apparently excellent examples of epidermophytosis with epidermophytids, in patients who gave negative reactions to intradermal injections of trichophytin. This contradicts a cardinal criterion for a diagnosis of epidermophytid.

15. Sicoli, A.: Ann. de dermat. et syph. **5**:69, 1924.

16. Ormsby, O. S., and Mitchell, J. H.: Ringworm of Hands and Feet, J. A. M. A. **67**:711 (Sept. 2) 1916.

17. Mitchell, J. H.: Amycotic Dermatoses Simulating Ringworm and Erosio Interdigitalis Blastomycetica, Arch. Dermat. & Syph. **19**:659 (April) 1929.

4. The specificity of trichophytin is still debatable.

5. In view of the present rather broad conception of palmar and digital epidermophytid, there is no reliable means for distinguishing absolutely between it and eczema (of undetermined origin) which may be coincidentally present with tinea pedis.

DISCUSSION BY CHARLES M. WILLIAMS, M.D.

The preceding paper has raised several questions for which as yet there is no certain answer; and although it cannot claim to be the final word, its detailed report of careful observations is a valuable addition to the scanty knowledge. There are several statements, however, which require comment. In the first place, the lesions may be trichophytids and yet contain fungi, at least in the very early stages. Such findings have been reported in typical transient lichenoid trichophytid and in transient vesicular trichophytid of the foot. The essential feature of trichophytid is the allergy, the altered sensitivity, which permits a minute amount of a fungus, or even a toxin, to produce a conspicuous lesion. Local sensitization to trichophytin, as recorded in case 34, is interesting and is in accord with Pirquet's [18] observation that the skin of his left arm, which he habitually used for experiments, was sensitive to tuberculin in a dilution of 1:1,000, while the skin of the right arm was negative to tuberculin ten times more concentrated.

The author's contention that many cases now diagnosed as epidermophytosis or epidermophytid have no connection with tinea is undoubtedly correct. The diagnosis is badly overworked. It is also true that a positive trichophytin reaction is no proof that the eruption on the patient's hands is in any way related to tinea, just as it is true that a positive Wassermann reaction is no proof that the scabies from which a patient suffers is due to syphilis. Like all laboratory tests—and like all other symptoms—the positive reaction to trichophytin is only one piece of evidence, to be weighed in connection with the others. The positive reaction may be due to a former, extinct infection. Amberg [19] mentioned a case in which the reaction remained positive for twenty-nine years after deep tinea. A negative reaction to trichophytin in cases in which fungi may be recovered from the feet is probably common. When it is observed in a patient who has dermatitis of the hands, it is evidence that the dermatitis is not trychophytid, but it is not conclusive evidence. In such a case, the sensitization may be localized in the hands. For example, I have seen transient trichophytid of the hands and feet in a case of tinea of the groins and axillae in which there was no trichophytid of the trunk, except in the immediate neighborhood of the axillae. Cases have been reported of transient trichophytid of the hands or the feet in which only one of the extremities harbored an active infection. Also, the skin may be sensitive to the patient's own organisms and their toxins, not to those produced in vitro. Many a patient with gumma has a negative Wassermann reaction.

The whole question is still obscure. The existence of acute transient trichophytid of the hands and feet is, I think, established beyond dispute. Whether any of the chronic eruptions of the hands are also trichophytids may be disputed, but I believe that the weight of evidence favors this diagnosis in a certain number of cases. I have learned no certain way of distinguishing these cases from the others.

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18. Pirquet, quoted by Cranston-Low: Anaphylaxis, New York, William Wood & Company, 1925, p. 194.

19. Amberg: J. Exper. Med. **12**:435, 1910.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

DRY GANGRENE OF THE FACE. SILBER C. PEACOCK, Am. J. Dis. Child. **45**:815 (April) 1933.

The author describes a rare case of dry gangrene of the face in a girl 18 months of age. The entire nose, a portion of each cheek and the whole upper lip, together with some gum tissue which held the central incisor tooth on the left side, were involved by the gangrenous tissue, which underwent mummification. The condition occurred subsequent to a mastoid infection followed by an abscess of the throat. The literature is reviewed.

ARGYRIA FROM THE USE OF COLLOIDAL SILVER IODIDE INTRANASALLY. MAX R. WOODWARD, Am. J. Dis. Child. **45**:1046 (May) 1933.

Three cases of argyria are reported in children following the excessively prolonged use of neosilvol given intranasally.

TOTAL UNILATERAL HYPERTROPHY. JOSEPH GLANZER, Am. J. Dis. Child. **45**:1056 (May) 1933.

An unusual case of total unilateral hypertrophy is reported. There were a large, flat, port wine nevus in the lumbosacral region and extensive purple mottling over the entire chest, abdomen and back. Of forty cases of this condition reported in the literature, cutaneous abnormalities were present in nearly 50 per cent.

CHEMICAL ALLERGY AND NIRVANOL SICKNESS. BELA SCHICK, HARRY SOBOTKA and SAMUEL PECK, Am. J. Dis. Child. **45**:1216 (June) 1933.

Observations concerning the chemical production of a disease resembling serum sickness are made by the authors. Nirvanol (phenyl-ethyl-hydantoin) has been used for about five years in the treatment of children suffering from chorea. In the majority of cases so-called nirvanol sickness occurs with the development of a syndrome characterized by an incubation period, fever, rash, edema, leukopenia and relative lymphocytosis, lymphadenopathy and other symptoms. The allergic features of the syndrome are discussed briefly.

THE TUBERCULIN PATCH TEST. MAURICE GROZIN, Am. J. Dis. Child. **46**:17 (July) 1933.

The tuberculin patch test described by the author is made by moistening a piece of adhesive plaster with 1 or 2 drops (0.06 or 0.1 Gm.) of old tuberculin (Koch) and applying it to the skin, which has previously been cleaned with ether. A piece of adhesive plaster without tuberculin may be used as a control. A positive reaction is indicated by redness studded with papules and vesicles. In a series of 176 cases this tuberculin patch test was carried out simultaneously with the Pirquet test. The results of the patch test compared favorably with those of the Pirquet test as to reliability. As advantages over the Pirquet test, the author mentions painlessness, no need of instruments, lack of danger of infection, simpler technic, less time and ease of interpretation.

BACILLUS PYOCYANEUS IN CHILDREN. J. W. EPSTEIN and A. B. GROSSMAN, Am. J. Dis. Child. **46**:132 (July) 1933.

This article is a résumé of the infections caused by Bacillus pyocyaneus in children. Among the infections of the skin mentioned are those about the umbilicus in the new-born and deep necrotic ulcerations termed ecthyma gangraenosum.

Cutaneous lesions and infected wounds due to Bacillus pyocyaneus are successfully treated by local applications of 1 per cent solutions of acetic acid or dilute solutions of hydrochloric acid (from 10 to 20 drops [0.6 to 1.2 Gm.] to 1 pint [470 cc.] of water).

ANDERSON, Los Angeles.

PRESENT DAY TECHNIQUE FOR THE STUDY OF HUMAN CAPILLARIES. A. W. DURYEE and I. S. WRIGHT, Am. J. M. Sc. **185**:664 (May) 1933.

A description is given of all the newest apparatus used in studying the blood flow in human capillaries. The mechanical devices consist of photographic apparatus, apparatus for the determination of capillary pressure, the temperature of the skin, capillary permeability and fragility, the rate of blood flow and the relative time of flow and stagnation.

EFFECT OF CHLORINATED SWIMMING-POOL WATER ON FUNGI OF TOE RINGWORM. DOROTHY SPRING, Am. J. M. Sc. **185**:775 (June) 1933.

In these experiments scrapings proved to contain fungi were immersed in the chlorinated water of a swimming pool for varying periods. Examination of the fungi after removal from the water showed that they were alive as long as one and a half hours, but no growth resulted after two hours or more of immersion. This would be sufficient to destroy any fungi remaining in the pool on detached pieces of skin. Scrapings taken from persons with proved cases of ringworm of the toes after a thirty minute period in the pool were all positive, showing that the water of the pool did not destroy the fungi between the toes.

TRANSFUSION SYPHILIS. C. L. CUMMER, Am. J. M. Sc. **185**:787 (June) 1933.

Cummer adds two cases of syphilis following transfusion to the number of cases reported and discusses the importance of repeated examinations of the blood of donors regarding the presence of syphilitic infection. The examination should be physical as well as serologic.

JAMIESON, Detroit.

CERTAIN UNSOLVED ASPECTS OF SYPHILITIC INFECTION SPECIALLY REFERRING TO THE POSSIBLE EXISTENCE OF SPIROCHAETA PALLIDA CARRIERS. W. E. COUTTS, Am. J. Syph. **17**:161 (April) 1933.

The author believes, on the evidence of certain clinical facts, that persons with latent syphilis may become active carriers of Spirochaeta pallida and cites two interesting cases to illustrate his point. Such circumstances would explain certain cases of syphilitic infection in which no apparent infective lesions can be found on the suspected person.

THE INFLUENCE OF RETICULOENDOTHELIAL "BLOCKADE" AND SPLENECTOMY UPON EXPERIMENTAL TRYPANOSOMIASIS AND SYPHILIS AND THE CHEMOTHERAPEUTIC PROPERTIES OF ARSPHENAMINE AND NEOARSPHENAMINE. JOHN A. KOLMER, JAY F. SCHAMBERG and BERNARD MADDEN, Am. J. Syph. **17**:176 (April) 1933.

The authors performed an interesting series of experiments concerning the rôle of the reticulo-endothelial system and spleen in experimental trypanosomiasis and syphilis and also concerning the chemotherapeutic properties of arsphenamine and neoarsphenamine. They produced partial blockade of the reticulo-endothelial system of rats and rabbits by intravenous injections of india ink. In rats this partial blockade slightly increased resistance to infection with Trypanosoma equiperdum and had no demonstrable effects on the trypanocidal activity of arsphenamine or neoarsphenamine. In rabbits there was no appreciable effect on infection with Spirochaeta pallida and no demonstrable effects on the spirocheticidal properties of arsphenamine or neoarsphenamine. Splenectomy in rats had no effect

on the development and course of infection with T. equiperdum, but it reduced the trypanocidal activity of arsphenamine and neoarsphenamine. Splenectomy in rabbits had no effect on the course of acute testicular syphilis, but it increased the spirocheticidal activity of arsphenamine.

It is apparent that splenectomy profoundly influences the trypanocidal and spirocheticidal activity of neoarsphenamine and arsphenamine.

CONTACT INFECTION OF RABBITS IN EXPERIMENTAL SYPHILIS. J. F. MAHONEY and K. K. BRYANT, Am. J. Syph. **17**:188 (April) 1933.

The authors record observations made on a large series of animals exposed to syphilitic infection by contact only. An assured exposure of the genital mucosa for a period of one hour was secured by inserting into the preputial sac a small pledget of cotton saturated in an emulsion containing Spirochaeta pallida in large numbers. Primary lesions, which were positive on dark-field examination, developed in twenty-seven of thirty animals, or 90 per cent, on or adjacent to the exposed area. The incubation period ranged from twenty-six to ninety-six days, with an average of forty-one days.

Based on the observation of sixty-six animals, the primary lesions were divided into two general classes: the internal class and the external class. The first group embraced those which occurred on the mucous lining of the preputial sac and the covering of the penis. The external group included the lesions which involved the cutaneous aspect of the preputial sac and the adjacent genital structures. The lesions observed were about equally divided between the two groups. Of the internal group, the earliest evidence of disease was a poorly defined erythema, which in five instances receded completely, the animals showing no further evidence of infection. The syphilitic nature of these changes was proved by the demonstration of Spirochaeta pallida in biopsy material taken from the site of the lesion. Progressive penile lesions developed in many animals, with swelling of the penis. In some animals a distinct papule formed, with central necrosis; in others the process became more diffuse, with necrosis and overlying grayish membrane. In the case of the external lesions, it was believed that the site of the sore did not accurately indicate the portal of entry of the organism. The authors believe that in the animals with preputial cutaneous lesions the primary penetration probably took place through the mucous surface and that an unknown factor determined the face of the membrane on which the outward manifestations would appear.

The early lesions on the cutaneous aspect of the preputial sac were small papules which increased in size, becoming "shotty" and finally definitely necrotic, with a membrane or crust over the ulcerating area. A few lesions did not progress beyond the papular stage. In two animals multiple lesions were observed.

It is problematic whether the atypical primary manifestations of the disease which were noted in this type of contact infection in rabbits may serve as an explanation of the not infrequent instances in human beings in which a patient with a syphilitic disease is honestly unaware of the time or the site of the original infection.

The use of inguinal adenopathy as a diagnostic sign was of little value in this series. In only a few instances, and then only in the presence of well defined chancres, could the inguinal nodes be satisfactorily palpated.

THE VASCULAR PERMEABILITY OF SYPHILIS. PAUL D. ROSAHN, Am. J. Syph. **17**:194 (April) 1933.

The author reports the results of certain experiments on the vascular permeability of syphilitic lesions of the rabbit as determined by intravital staining. Neutral red was injected intravitally into syphilitic rabbits; the dye was fixed in situ immediately following injection. The primary orchitis and metastatic orchitis were studied.

Syphilitic lesions of the nodular, indurated type failed to be stained and were sharply demarcated from the surrounding red color of unaffected tissue by their

white appearance. The failure of the tissues to stain coincided with the development of obliterative endarteritis, which was present in varying degrees in each instance. It is suggested that the dye penetrates the lesion by a process of diffusion through the vessels at the periphery and that therapeutic agents introduced into the blood stream operate in the same manner.

A Comparative Pharmacologic Study of Absorption, Distribution and Excretion of Injectable Bismuth Preparations. M. R. Thompson, G. E. Cwalina, C. T. Ichniowski and Bertran S. Roberts, Am. J. Syph. **17**:205 (April) 1933.

Five typical bismuth preparations—an oil preparation and four different aqueous preparations—were subjected to comparative pharmacologic study as to the rate of absorption from the site of the injection, distribution in the kidneys and liver, urinary excretion, irritation at the site of injection and toxicity.

Only very small amounts of bismuth remained unabsorbed after the first week, although the preparations varied in their absorption rate. The preparations which were absorbed the fastest showed the greatest toxicity. Following toxic doses the greatest destruction of tissue occurred in the liver and kidneys. Distinct doubt is thrown on the desirability of too rapid absorption of bismuth preparations because of a correspondingly rapid rate of excretion and the attendant danger of overburdening the kidneys and liver. It does not follow that a comparatively rapid absorption of bismuth preparations will result in a more effective concentration against syphilis, since the excess amounts provided thereby may be quickly taken up by the organs of storage and excretion. There is a possibility that the more slowly absorbed preparations would prove fully as effective, with a lesser tendency toward toxicity and a more prolonged effect from each dose. Two of the preparations produced definite evidence of irritation of the muscle when injected in large doses, but in none of the preparations was this irritation of sufficient magnitude to prove serious when the drug was used clinically in the customary doses.

Standardization of the Complement Fixation Test for Syphilis. Ruth Gilbert, Am. J. Syph. **17**:238 (April) 1933.

This is a lengthy article which sets forth the proposed plan for a standard procedure in the performance of the complement-fixation test for syphilis. Pertinent data from communications received from well known serologists regarding the plan are listed alphabetically at the end of the article. Reuter, Milwaukee.

Advances in the Diagnosis and Treatment of Thrombo-Angiitis Obliterans. Samuel Perlow, Ann. Surg. **98**:43 (July) 1933.

In this article the author evaluates the various tests for circulatory efficiency of the lower extremities which may be of aid in establishing a diagnosis of thrombo-angiitis obliterans, such as ischemia on elevation with rubor on depression of the extremity, and Buerger's estimation of the angle of circulatory sufficiency. The latter test is based on the supposition that the normal leg, when elevated at right angles to the supine patient (from 180 degrees to the normal vertical position), retains its color. When circulation is impaired, the foot blanches in this position. The leg is gradually depressed in this type of patient, and the angle at which normal color returns is noted. In thrombo-angiitis obliterans this angle is usually about 60 degrees and is seldom above 90 degrees. The author considers surface temperature of little reliability in the diagnosis of the disease, but considers the use of the oscillometer of distinct value. The intradermal saline test and the histamine test are also briefly described. In regard to treatment, discontinuing the use of tobacco is advised, in addition to rest in bed and therapy with heat, with diathermy or quartz light, if indicated. Alternate elevation and depression of the

extremity, as advised by Buerger, and contrast baths are also suggested as being of distinct value. The merits of intravenous injections of a 5 per cent solution of sodium chloride, foreign protein therapy and various operative procedures are also discussed.

PERIPHERAL VASOCONSTRICTION BY TOBACCO AND ITS RELATION TO THROMBO-ANGIITIS OBLITERANS. WALTER G. MADDOCK and FREDERICK A. COLLER, Ann. Surg. **98**:70 (July) 1933.

Studies carried out on young adults who smoked cigarets demonstrated a consistent increase in the blood pressure and pulse rate and a decrease in the temperature of the skin of the fingers and toes. Nicotine injected intravenously in doses comparable to that theoretically absorbed from the cigarets during the experiments produced analogous changes. Greater effects were noted from inhaling than from ordinary smoking and from rapid smoking than from slow smoking. The effects lasted for about thirty minutes after the smoking was stopped and were of longer duration in the toes than in the fingers. In two patients with thrombo-angiitis obliterans smoking produced the same cardiovascular response as in the normal subject; the effect in one patient lasted forty-five minutes. The authors do not advance the effects of nicotine as an etiologic factor in the production of thrombo-angiitis obliterans, but recommend its withdrawal in patients already afflicted with the disease.

WIEDER, Milwaukee.

SYPHILIS OF THE STOMACH, WITH SPECIAL REFERENCE TO THE SIGNIFICANCE OF SPIROCHETES. H. A. SINGER, Arch. Int. Med. **51**:754 (May) 1933.

The question is discussed in detail whether spirochetes found in the wall of a gastric ulcer can be positively distinguished as Spirochaeta pallida. According to the author, most of the "positively" identified organisms in cases that have been reported are probably spirochetes of oral origin, which are often found in relatively large numbers and are frequently accompanied and preceded in their invasion by bacterial organisms. The author reports a case in which he thinks that the condition was possibly a nonsyphilitic granuloma in a syphilitic patient, although spirochetes were found in the gastric wall. The diagnosis in cases of this nature should rest on clinical, laboratory, therapeutic and macroscopic anatomic observations.

TREATMENT OF NEUROSYPHILIS: REVIEW OF RESULTS IN SIX HUNDRED AND EIGHTY PATIENTS. H. H. HOPKINS, Arch. Int. Med. **52**:66 (July) 1933.

An analysis of the results obtained in the treatment of 480 patients with neurosyphilis, who were under observation for two years or more, and also of 200 who died while under observation is presented. The cases were divided into the following classes: early neurosyphilis, diffuse late syphilis, dementia paralytica (including taboparesis), tabes dorsalis, optic atrophy and vascular neurosyphilis. They were also charted according to the form of treatment: poor, routine, intensified routine, routine treatment plus subdural serum treatment, routine treatment plus tryparsamide and routine treatment plus malaria.

Charts show the percentage of the results of treatment which may be briefly summarized as follows: An intensified routine antisyphilitic treatment with arsphenamine gave the best results in early neurosyphilis, but in the diffuse late variety it was found to be inferior to arsphenaminized serum given subdurally. In diffuse late neurosyphilis tryparsamide gave results almost as good as those produced by the serum. In dementia paralytica, the best results followed treatment with malaria. This was also true in tabes. Tryparsamide also gave beneficial results in tabes, and both these forms of treatment were superior to routine treatment. Optic atrophy was most successfully treated and arrested by subdural injections of arsphenamized serum.

THE USES AND DANGERS OF COSMETICS. ALICE CARLETON, Brit. M. J. **1**:999 (June 10) 1933; R. M. B. MACKENNA, Brit. M. J. **1**:1128 (June 24) 1933.

In the *British Medical Journal* of May 17, 1930 (abstr., ARCH. DERMAT. & SYPH. **22**:514 [Sept.] 1930), there was an excellent article by MacKenna on modern cosmetic preparations in which he called attention to the ill effects sometimes produced by their prolonged and continuous use. Carleton, in her article, questions the validity of some of MacKenna's claims. She was unable to substantiate his observations, and, in general, she thoroughly endorses the use of cosmetics, especially the greasy preparations. MacKenna, then, in answer, critically reviews Dr. Carleton's paper and in a convincing manner thoroughly annihilates her position. He makes the statement that fats tend to block the sebaceous and sweat glands, thus facilitating the formation of comedones, and causing acne vulgaris to develop. He maintains that a skin is not clean which is wiped with a cold cream, massaged with vanishing cream and then powdered, being left coated with a layer of grease to which dust as well as toilet powder readily adheres. He agrees that creams may be of use, but states that their continuous use carries with it possibilities for harm. Both articles give formulas for some of the common preparations.

RATTNER, Chicago.

BACTERIAL PSEUDOMYCOSES. A. CASTELLANI, J. Trop. Med. **36**:141 (May 15) 1933.

One form of pseudomycoses is that caused by Micrococcus myceticus. In this condition the first lesion is a red, raised spot which appears rather suddenly and rapidly enlarges to the size of a half dollar. Lymphangitis develops simultaneously, with a rise in temperature to 104 F. The temperature returns to normal within from twenty-four to forty-eight hours, but the lesion persists, and after a few days or weeks other spots gradually make their appearance in the vicinity of the first. These infiltrated areas enlarge and soften, subsequently discharging pus and leaving indolent sinuses. The general appearance of the involved area resembles streptotrichosis. Two other types of pseudomycosis are described; in one the causative organism is Bacillus typhosus; the other is a form of dermatitis resembling blastomycosis but due to bacterial invasion.

JAMIESON, Detroit.

A PECULIAR CASE OF POROKERATOSIS MIBELLI WITH CORNEOMAS. G. VERROTTI, Gior. ital. di dermat. e sif. **74**:3 (Feb.) 1933.

This is a clinical and histopathologic study of an extensive case of porokeratosis with multiple keratotic accumulations which the author calls "corneomas." The histopathologic study demonstrated that the hyperkeratotic process, characteristic of this peculiar dermatosis, is the result of a granulomatous inflammation of unknown origin. This inflammatory process seems to begin in the sweat glands and reaches its maximum in the stratum subpapillaris. The author rejects the theory that the condition is nevoid in character.

PATHOGENESIS OF NECROBIOSIS LIPOIDICA DIABETICORUM URBACH-OPPENHEIM. E. BALBI, Gior. ital. di dermat. e sif. **74**:14 (Feb.) 1933.

In a recent monograph by Urbach in Jadassohn's handbook concerning cutaneous diseases related to disturbances of lipoidal metabolism, a definite distinction is made between generalized and localized lipoidosis. In the first group are included xanthoma, extracellular cholesterinosis of Kerl-Urbach, Niemann-Pick's disease, Burger-Grütz lipoidosis, Gaucher's disease and lipoido-proteinosis of Urbach-Wiethe. In the second group are included lipoidal degeneration of the elastic tissue of Kriebich and necrobiosis lipoidica diabeticorum of Urbach-Oppenheim.

Necrobiosis lipoidica was reported for the first time by Oppenheim to the Vienna Dermatological Society in 1929 under the name of "a peculiar disseminated degeneration of the cutaneous connective tissue in a diabetic." There were disseminated

papules on the lower limbs and to a less extent on the trunk and upper limbs. These papules were wine-colored and small and firm on palpation. Coalescence was observed with the formation of larger elements and a variation in color from red to yellowish brown. Subsequently, these lesions underwent involution, the central part appearing sclerodermic or atrophic. Histologically Oppenheim noted an inflammatory reaction in the periphery of the lesions, and necrobiosis of the central involuting parts, with absence of elastic tissue. Reactions typical of hyaline, amyloid and colloid degeneration were lacking. Oppenheim concluded that the condition was due to degeneration of the connective tissue produced by diabetes. In 1932 Urbach presented an analogous case under the title of "Multiple Cutaneous Degenerations with Extracellular Deposits of Lipoids in a Severe Diabetic," and also "Necrobiosis lipoidica seu diabetica." In Urbach's case the necrotic foci were readily stained with sudan III, and his patient had a lipemia of 700 per cent and cholesterinemia of 270 per cent.

In this excellent article Balbi reports a typical case of this condition in a man, aged 55, with severe diabetes. He calls attention to the intense vascularitis present in the histologic picture and to the thrombotic formations. Clinically the cutaneous lesions were similar to those described by Oppenheim and Urbach, but in this case many lesions ended in central ulceration. Microchemical investigations confirmed the presence in the necrotic foci of phosphatids and neutral fats.

According to Balbi, the condition is due to the deposit in the tissues of the lipoids of the blood, through the primarily damaged walls of the vessels.

Uric Acid and Eczema. Uricacidemia and the Renal Elimination of Uric Acid in Patients Treated with Uric Acid. M. Comel, Gior. ital. di dermat. e sif. **74**:44 (Feb.) 1933.

Researches carried out by Comel to establish the nature of the metabolic changes concerning uric acid in patients suffering from eczema demonstrated that the amounts of uric acid in the blood and in the urine are very low. This may be explained by a possible retention of uric acid in the tissues or by an increased elimination through other emunctories.

The oral administration of uric acid does not materially alter the elimination of uric acid in the urine or the uric acid findings in the blood of patients with eczema. The intravenous administration of 1 Gm. of uric acid is followed by a remarkable increase of the uric acid in the circulating blood during several days and by a corresponding increase in elimination of uric acid in the urine. The amount of uric acid eliminated does not equal that administered through the veins, but it equals about 50 per cent of that amount. Patients with eczema, therefore, act like persons with gout in the presence of an excess of uric acid, retaining it in the tissues. Comel used the Folin and Denis method for the determination of uric acid, considering 3 mg. per hundred cubic centimeters as the maximum normal output.

Leprosy: Report of Three Cases, Particularly in Regard to the Presence of Bacillemia. G. B. Cottini, Gior. ital. di dermat. e sif. **74**:84 (Feb.) 1933.

Cottini reports three cases of acute leprosy in all of which he demonstrated Hansen's bacilli in the circulating blood. One of these patients, a young man, aged 18, had a generalized erythema nodosum.

[Erythema nodosum lesions are of common occurrence during acute attacks of leprosy. In Cuba cases of febrile erythema nodosum or erythema multiforme are always considered by me as of possible leprous nature, even in the absence of other symptoms of leprosy. Often the first manifestation of leprosy is an attack of erythema multiforme with nodular lesions. In these cases lepra bacilli can be found in the circulating blood during the acute attack, and the cutaneous lesions are always found teeming with acid-fast bacilli.]

THE CHARACTERISTICS ("CHARAKTERBILD") OF PATIENTS WITH NEUROFIBROMATOSIS. HEDWIG BLOTEVOGEL, Dermat. Wchnschr. **96**:361 (March 18) 1933.

The author found that in some instances neurofibromatosis may be a dominant characteristic in the heredity, while in other instances it may be a recessive one. The blood grouping of thirty patients with neurofibromatosis showed that more than the normal percentage fell in group A. Study of the fingerprints of twenty-seven of these patients showed a greater predominance of certain unusual features than occurs in normal persons. Anthropologic measurements demonstrated marked variations from the normal. Especially noteworthy were the large head and long extremities.

THE ALLERGIC NATURE OF PSORIASIS VULGARIS. PAUL FASAL, Dermat. Wchnschr. **96**:369 (March 18) 1933.

The author concludes that there is no evidence that psoriasis is an allergic condition. The treatment of four patients who reacted to pollen extracts by subcutaneous injection of these extracts was unavailing. It seems likely that in those instances in which benefit from such treatment has been reported, the effect was that of a nonspecific foreign protein rather than a specific desensitization.

PSORIASIS AND ARTHROPATHIA PSORIATICA. HARALD LOTZE, Dermat. Wchnschr. **96**:389 (March 25) 1933.

A patient was observed who had psoriasis and arthritis at different times, and finally both at the same time. It was noteworthy that the psoriasis differed from the usual type in the variation of the types of lesions present and in the distribution on the palms and soles and in the axillary and perineal regions. The arthritis was characterized by the varying pictures presented, some lesions suggesting primary chronic arthritis and some arthritis deformans or other forms.

THE MEASUREMENT OF THE CONSISTENCY OF THE SKIN IN VARIOUS CONDITIONS. E. M. LEWIN and B. N. MAJORSKY, Dermat. Wchnschr. **96**:395 (March 25) 1933.

The authors have constructed an apparatus by means of which the consistency of the skin can be measured. With this instrument they measured the consistency in various disorders, such as primary chancre, papular syphilis, epithelioma, lupus vulgaris and erythema induratum. They believe that changes in the values may be used to check the efficacy of treatment.

CUTANEOUS CHANGES IN ALEUKEMIC LYMPHADENOSIS. ARTHUR JORDAN and W. SCHAMSCHIN, Dermat. Ztschr. **66**:1 (March) 1933.

The authors review briefly the literature on aleukemia. They consider white blood counts up to 10,000, with relative lymphocytosis, as aleukemic. Counts of from 10,000 to 30,000 are classed as subleukemic and those above 30,000 as indicative of true leukemia. Two cases of aleukemia and two of subleukemia are described. In two of these prurigo lymphatica was noted; in one, prurigo lymphatica associated with erythroderma, and in one, simple pruritus. The diagnosis was based on generalized pruritus, the presence of nodules, adenopathy and relative lymphocytosis. Histologic examination confirmed the diagnosis in 2 instances. While the cutaneous changes alone are not sufficient to justify a positive diagnosis of aleukemia, they are often suggestive.

THE GENERALIZATION OF THE SYPHILITIC VIRUS IN EXPERIMENTAL SUPERINFECTION. EDOARDO BALBI, Dermat. Ztschr. **66**:11 (March) 1933.

Five persons with symptoms of late syphilis were reinfected with either the Truffi or the Nichols strain of Spirochaeta pallida. A "take" was obtained in

each instance. In two cases injection of tissue from the regional lymph nodes into rabbits produced typical syphilomas. The strain was then identified by infecting the animal after a suitable period with both strains. Immunity to the homologous strain in each instance indicated that the strain recovered was the one originally used in the experiment.

DEMONSTRATION OF TUBERCLE BACILLI IN THE CIRCULATING BLOOD BY LÖWENSTEIN'S METHOD IN VARIOUS FORMS OF TUBERCULOSIS OF THE SKIN, LUPUS ERYTHEMATOSUS AND GRANULOMA ANNULARE. JOSEF KONRAD, Dermat. Ztschr. **66**:30 (March) 1933.

Blood cultures were made by the Löwenstein method in 134 cases, 87 of tuberculosis of the skin, 43 of lupus erythematosus and 4 of granuloma annulare. A positive culture was obtained in 22 per cent of the cases. In 12 of the 43 cases of lupus erythematosus and in 2 of the 4 cases of granuloma annulare the cultures were positive, while only 1 of 25 cases of lupus vulgaris showed a positive culture. The incidence of positive cultures increased with the number of tests made in each case. The author states that further work must be done by the bacteriologists to prove that the organism obtained on culture is a true tubercle bacillus.

EXPERIMENTAL INVESTIGATIONS OF THE INCREASE AND DECREASE OF ABSORPTION BY THE SKIN. WILHELM MILBRADT, Dermat. Ztschr. **66**:37 (March) 1933.

The absorption of substances by the skin depends on the functional condition of the skin, on the method of application and on the substance applied. Irritation increases the permeability of the skin up to a certain point and then suddenly decreases it. The importance of the various factors is discussed at some length.

L. TAUSSIG, San Francisco.

BIOLOGIC ACTION OF GAMMA RAYS. AXEL WALLGREN, Acta radiol. **14**:111 (May) 1933.

This article is based on research carried out by the author at the Radiumhem in Stockholm, which is a continuation of similar work with roentgen rays and light rays. In this experiment he exposed neutrophilic leukocytes in direct preparations from normal blood at 37 C. at a minimum distance of 3 mm. to radium applicators containing thirty-four tubes, each of which contained 50 mg. of radium element, with a filter equal to 1 mm. of lead. Exposure to the rays for fifteen minutes immobilized some single granulocytes, which became active again after irradiation was stopped. After irradiation of from thirty to sixty minutes a great many became immobilized, but most of these recovered on cessation of irradiation. After fifty minutes, however, a number of cells were either dead or in the process of disintegration. With irradiation of from two to two and a half hours, most of the granulocytes were damaged, dead or in process of disintegration when the irradiation was stopped. These findings correspond with the author's previous experiments with gamma rays; the first demonstrable biologic effect of irradiation with light rays, roentgen rays or gamma rays is immobilization of the granulocytes, the structural changes appearing later. WIEDER, Milwaukee.

Society Transactions

DETROIT DERMATOLOGICAL SOCIETY

Regular Meeting, March 10, 1933

EMMETT C. TROXELL, M.D., *Presiding*

A CASE FOR DIAGNOSIS (LICHEN PLANUS?). Presented by DR. WILLIAM G. WANDER.

Mrs. E. F., aged 67, born in Scotland, has been anemic for several years and has taken solution of iron and ammonium acetate, U.S.P. She presents an eruption on the thighs of five weeks' duration, which first appeared on the external surface of the right thigh. She complains of no itching, but of occasional burning sensations in the older lesions. There is a symmetrical eruption of small, grouped, dusky red papules. There is a crusted area on the right upper eyelid, where radium was applied to an epithelioma of five years' duration. The Kahn reaction was negative.

DISCUSSION

DR. UDO J. WILE: The eruption is suggestive of aberrant pityriasis rosea, unusual in type and in localization. The duration has been short, and there is a tendency toward involution.

DR. HOWARD J. PARKHURST: The flat polygonal papules impressed me as being lesions of lichen planus, though paler than is usual, perhaps as a result of the anemia. I found no eruption in the mouth.

DR. ROBERT A. C. WOLLENBERG: I agree with the diagnosis of lichen planus. It is my impression that the lesions have been present for two or three months.

DR. JOHN A. HOOKEY: Around the borders of the eruption, about the knees, there are some typical papules of lichen planus.

DR. ROBERT C. JAMIESON: I found some atrophic areas on the thighs, and I thought that the duration was longer. I agree with the diagnosis of lichen planus.

DR. WILLIAM G. WANDER: The eruption has been present only four or five weeks. The lesions had a violaceous color yesterday which has faded. Some of the lesions look like those of lichen planus, and others suggest atypical psoriasis. The anemia may have something to do with the appearance.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. LOREN W. SHAFFER.

L. W., a man, aged 30, a janitor, presents an eruption of ten years' duration on the dorsum of the left hand. It began as a nodule, which enlarged slowly, with partial healing and central scarring. New nodules developed at the periphery, and the entire dorsum of the hand and the proximal portions of the fingers became involved. Some of the peripheral nodules are lentil-sized and conical, while others are larger, flatter and crusted. All are dry. Pus has been present at times, but never to a marked degree. The area is not verrucous. The Wassermann reaction was negative.

DISCUSSION

DR. ARTHUR E. SCHILLER: There is some resemblance to a mycotic infection or to hypertrophic lichen planus.

DR. LOREN W. SHAFFER: An old biopsy report confirmed the diagnosis of tuberculosis verrucosa cutis.

DR. GEORGE VAN RHEE: This case was diagnosed and treatment was given seven or eight years ago at Harper Hospital. The lesions were more verrucous at that time.

DR. CYRIL K. VALADE: Carbon dioxide snow and the roentgen rays were used in the treatment of this patient at Harper Hospital.

PAPULONECROTIC TUBERCULID. Presented by DR. LOREN W. SCHAFFER.

G. B., a woman, aged 29, born in Scotland, has been in good general health, except for moderate cervical lymphadenitis on the left side of six months' duration. On the elbows, knees and fingers there is a papular eruption, with pitted scars, of nine years' duration. The appearance of the tonsils suggests a pathologic condition. Roentgenologic studies of the chest revealed no evidence of pulmonary tuberculosis. The Wassermann reaction was negative.

DISCUSSION

DR. HARTHER L. KEIM: I agree with the diagnosis of papulonecrotic tuberculid.

DR. ROBERT C. JAMIESON: The patient lived on a farm during the first nine years of her life, and it is possible that the tuberculous infection is of the bovine type. One sees fewer of these cases than formerly.

DR. UDO J. WILE: In our clinic my associates and I have seen no papulonecrotic tuberculids for two or three years, although we have encountered many other forms of tuberculosis.

LYMPHOBLASTOMA (?). Presented by DR. ROBERT C. JAMIESON.

E. C. K., a man, aged 49, employed in a factory, has had no major ailments, but complained of some gastric distress and had dermatophytosis pedis eight years ago. He presents a dry, pruritic eruption of two years' duration. The condition appeared first on the front of the left leg, on the inner surface of the lower third of the leg and on the instep. It yielded to local medication and roentgen irradiation but recurred a year later in the form of small and large irregular patches of lichenoid eczema on the dorsa of the hands and on both forearms, simulating occupational dermatitis. This eruption recurred at intervals, later being accompanied by larger areas on the trunk and the legs. The involved areas are dry, somewhat shiny and irregular in size, shape and outline. Pruritus is pronounced at times. On examination, the epitrochlear, axillary and inguinal lymph nodes were palpable. The differential blood count was normal. The urine was normal. The Wassermann reaction was negative. The patient was examined at Ann Arbor two years ago, but no definite pathologic observations were made.

DISCUSSION

DR. GEORGE H. BELOTE: The rather seborrheic appearance of the eruption, its scaliness, the long duration and the enlargement of the lymph nodes favor a diagnosis of lymphoblastoma.

DR. CYRIL K. VALADE: I agree with the diagnosis of lymphoblastoma.

DR. ROBERT C. JAMIESON: What is to be done for the patient? Roentgen radiation has been used only over certain severely involved areas. There may have been an occupational factor at times. I think that the condition will eventually become definite lymphoblastoma.

DR. HARTHER L. KEIM: Even when these cases are advanced, the condition may at times undergo involution and the patient become practically well.

DR. UDO J. WILE: One of the patients observed by my associates and me at Ann Arbor presented all of the characteristics of lymphoblastoma. He has now apparently recovered and is working as a locomotive fireman. I do not feel that our treatment accomplishes these good results. The patients have to be kept under observation for many years.

DR. ARTHUR E. SCHILLER: Might not fever therapy be helpful in these cases?

DR. JOHN A. HOOKEY: At the Mayo Clinic there was a patient with mycosis fungoides and syphilis of the central nervous system. Following inoculation with malaria the eruption subsided for a short time.

A CASE FOR DIAGNOSIS (MULTIPLE GUMMAS?). Presented by DR. LOREN W. SHAFFER.

C. C., a man, aged 54, states that two months ago he noticed a small papule on the septal side of the left naris. It rapidly became pustular, and a destructive necrotic process ensued. The lower portion of the septum and the left ala nasi have been destroyed. The lesion presents a ragged border with little induration or granulomatous infiltration. It is tender, and pus exudes under pressure. The presence of acid-fast organisms was revealed by biopsy. There is a necrotic ulcer the size of a small coin posteriorly on the left side of the lower gum. The Wassermann reaction was positive.

DISCUSSION

DR. HARTHER L. KEIM: I favor a diagnosis of multiple gummas. The patient's age, the duration of the condition and the histologic picture are compatible with that diagnosis.

DR. GEORGE H. BELOTE: The appearance of the margin of the lesion suggests carcinoma, but the histologic picture favors a diagnosis of syphilis, as do the multiplicity and the rapid growth of the lesions. I agree with Dr. Keim.

A CASE FOR DIAGNOSIS (PEMPHIGUS OF SENEAR-USHER TYPE?). Presented by DR. HARTHER L. KEIM.

Mrs. I. H., has always been in good general health. Three years ago a red, crusted area appeared on the scalp over the left ear. It persisted and slowly enlarged. Two years later bullae appeared over the lower part of the back, remained for several months and disappeared. Three months ago small lesions appeared on the upper part of the trunk, and the remains of several have persisted. New lesions have been appearing on the scalp for several months, increasing in size and number. Three weeks ago six vesicles appeared on the left cheek and healed promptly. The chief subjective symptoms have been pain and extreme tenderness of the lesions.

On examination, the patient, a well nourished woman, presented crusted erythematous lesions on the scalp and on the anterior surface of the trunk. The lesions were bullous originally, but had become covered with a dry adherent crust. Over the left ear on the scalp there was a large erythematous lesion, sharply raised, firmly infiltrated and at times heavily crusted. The remaining lesions on the scalp were smaller and erythematovesicular, with a thick, tenacious, yellow crust.

DISCUSSION

DR. ARTHUR P. R. JAMES: Some of the lesions on the scalp resemble those of psoriasis.

DR. LOREN W. SHAFFER: I feel that the condition is possibly an atypical form of pemphigus.

DR. HOWARD J. PARKHURST: I agree with Dr. Shaffer.

DR. CYRIL K. VALADE: The possibility of dermatitis factitia should be considered.

DR. ROBERT A. C. WOLLENBERG: Were any fungi found in the lesions?

DR. HARTHER L. KEIM: At first I thought of a bromide or an iodide eruption, and later I felt that the condition might prove to be an early example of the Senear-Usher syndrome. About four weeks ago the large lesions on the scalp resembled those of weeping lupus erythematosus or a moist seborrheid.

MANHATTAN DERMATOLOGIC SOCIETY

M. B. PAROUNAGIAN, M.D., *Secretary*

March 14, 1933

FRED WISE, M.D., *Chairman*

NEVUS LINEARIS. Presented by DR. HOWARD FOX.

A salesman, aged 26, born in the United States, has an eruption from which he has suffered since birth. It is situated on the left side of the neck, the left supraclavicular region, the center of the sternum, the middle third of the back, the center of the forehead, the nose and the tongue. The lesions are brownish-yellow, papillomatous and verrucous elevations forming continuous or broken linear bands in places and coalescing to form solid areas in others. A narrow linear band extends from the forehead to the tip of the nose, and a similar band extends along the center of the sternum. On the back are several markedly thickened V-shaped bands forming acute angles with the spinal column. The left side of the greater part of the dorsum of the tongue shows a closely packed mass of soft acuminate folds. On the left side of the neck there are a severe chronic radiodermatitis with numerous keratoses and one crusted lesion the size of an almond, suggesting an epithelioma. Ten years ago the patient was treated with the roentgen rays at a hospital in New York. The lesion on the tongue causes a slight defect in speech. The patient is of medium size and of fair complexion. A few of the most conspicuous lesions on the face have recently been treated by electrodesiccation.

DISCUSSION

DR. GEORGE M. MACKEE: I do not think that the roentgen rays or radium is indicated in this case. I do not think that it is possible to obtain eradication of the nevus except with a much larger dose of these agents than it is justifiable to give. There is a beginning epithelioma, caused, I believe, by the treatment attempted in the past. I suggest that an extensive two-stage plastic operation be performed. The nevus and the damaged skin should be removed and replaced by a tubular graft.

DR. DAVID L. SATENSTEIN: Nevi consist of abnormally placed normal tissue. In order to obtain clinical results with either the roentgen rays or radium sufficient intensity to cause either destruction or absorption of normal tissue is necessary. As these agents are not selective in their action, all the exposed parts are affected, usually resulting in a condition of prematurely senile skin with or without other damage: so-called radiodermatitis or other sequelae of irradiation. Such prematurely senile skin is liable to undergo malignant changes. Changes of this nature are in evidence in this case. Therefore, I should suggest radical removal of the affected part, with subsequent plastic operation.

DR. ANDREW J. GILMOUR: Would any one advise gradual removal of the lesion on the tongue with the electric needle?

DR. GEORGE M. MACKEE: Electrosurgery is permissible in treating a nevus of this type, but in this particular case I should prefer a plastic operation.

DR. HOWARD FOX: I am glad to receive the suggestion as to the advisability of a plastic operation for removal of the injured skin. I think that it is possible that one area has already undergone malignant change, and I agree that unless a radical plastic operation is performed the patient is liable to suffer from cancer in the future. In order to gain the patient's confidence, I first treated the conspicuous lesion on the nose and suggested that his speech might be helped by treating the mass on the tongue by electrodesiccation.

A Case for Diagnosis (Telangiectases of the Sides of the Neck in a Woman). Presented by Dr. Fred Wise.

A woman, aged 46, from the clinic of the New York Post-Graduate Medical School and Hospital, applied for treatment on March 14, 1933. Two years ago she noticed a discoloration on both sides of the neck, below the lobes of the ears, which she stated appeared simultaneously with the beginning of the menopause.

Examination revealed fine telangiectatic patches on both sides of the neck, which were devoid of pigmentation and were not associated with reticulation or beginning atrophy. The surface of the lesions showed no scaling or other evidences of inflammation. The appearance resembled that of a weather-beaten skin. The affected areas were approximately 4 inches (approximately 10.2 cm.) in diameter and were sharply demarcated, with distinct concave borders on the lateral surfaces of the neck; they shaded off gradually toward the mastoid processes and had no clearly defined border posteriorly. The skin of the adjacent portions of the neck exhibited no evidence of a weather-beaten condition, being normal in color and consistence and offering a sharp contrast to that of the telangiectatic areas.

A tentative diagnosis of poikiloderma of Civatte was suggested, but because of the absence of pigmentation and reticulation this diagnosis was discarded.

DISCUSSION

Dr. George C. Andrews: I think that the diagnosis of poikiloderma is the proper one for this case. "Peasant's neck" often occurs in persons whose skin has been exposed to the sun over a period of time.

Dr. Joseph J. Eller: I have seen a similar condition several times in women whose skin has been exposed to the sun and the elements, and I have always thought that it was acne rosacea with telangiectasis.

Dr. Isadore Rosen: I agree with the diagnosis of poikiloderma of Civatte. While the clinical features in this case are not absolutely typical of this disease, the age of the patient, the appearance of the lesions and their location and persistence lead me to entertain this diagnosis.

Dr. Howard Fox: This is a clinical picture with which all of us are familiar, although the condition may have been called by names other than poikiloderma. I think that it is fairly common.

Dr. Andrew J. Gilmour: One point in the history is curious: The patient states that when she bends over, when she walks up and down stairs and also when she touches the neck she has pain.

Dr. George M. MacKee: The diagnosis of poikiloderma is tenable. I think that in Civatte's cases there was a more uneven and a more widespread telangiectasis. One frequently sees people with telangiectasis of the neck which is supposedly due to exposure to the elements, but this case is different because of the sharp margins. The erythema in the center of the chest is probably due to a vasomotor disturbance and is unrelated to the telangiectasis of the neck.

Dr. Paul E. Bechet: I have often observed an eruption on the back and the sides of the neck closely resembling the lesions in this case, in patients who have been frequently exposed to sunlight. The patient under discussion told me that she lived in Westchester and that she spent the greater part of the summer in the garden. It is possible, therefore, that the present eruption is of actinic origin.

Dr. Max Scheer: I do not think that the eruption is due to exposure to the elements and to sunlight on account of the sharp outline, the scalloped borders and the absence of lesions on adjoining areas which must have been similarly exposed. Since the neck as well as the face is a flush area of the skin it is theoretically possible for acne rosacea to occur in this region, although I have never seen this phenomenon. The presence of erythema and telangiectasis alone, without reticula-

tion, pigmentation or atrophy, makes the diagnosis of poikiloderma of Civatte very unlikely in this case, especially as one would expect to see some changes of this nature after two years.

DR. FRED WISE: I think that the condition is exceedingly common. Although I believe that poikiloderma of Civatte should be mentioned, I doubt that it is the correct diagnosis. Reticulation, pigmentation and atrophy are not present. I cannot conceive of sharp marginated lesions such as the patient presents being due to the sun and wind or to exposure to inclement weather. I know that the same condition is found in males, but I do not know at what age and under what conditions it occurs.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. HOWARD FOX.

S. F., a girl, aged 17, the operator of a machine, who was born in the United States of Italian parents, has suffered for two months from an eruption which consists of well defined superficial reddish patches with a few fine adherent scales. There is no appreciable thickening of the skin on palpation, and atrophy is not present. Most of the eruption is situated on the nose and the upper part of the cheeks; the left eyebrow, the chest, the chin, the neck and the extensor surface of the right forearm are involved to a slight extent. There is a moderate enlargement of the lateral cervical, axillary and inguinal glands. The tonsils have been removed, and there is one carious molar. The patient had edema of the hands and feet and pains in the joints which responded to treatment with salicylates. Examination of the chest showed diminished breathing in the upper thirds anteriorly and posteriorly and a slight impairment of the resonance in the left apex. On percussion, dulness was found to be increased in the left side of the upper portion of the heart, and there was accentuation of the second pulmonic sound. There were no murmurs and no râles.

Examination of the blood showed 4,200 white cells and 3,200,000 red cells. The differential count showed 56 per cent polymorphonuclears, 8 per cent mononuclears, 32 per cent lymphocytes and 4 per cent transitionals. The urine contained a faint trace of albumin. A sedimentation test of the blood gave a high reading (50 mm. in one hour). At the time of the patient's last visit the temperature by mouth was 99.7 F. at 10 a. m. She was well nourished, and her general condition was apparently good.

DISCUSSION

DR. PAUL E. BECHET: The eruption is typical of lupus erythematosus disseminatus. In reference to aurotherapy in this type of lupus, I should say that gold preparations are not absolutely contraindicated, but they must be used with great caution. In my experience, it is in the disseminate type of lupus that the most brilliant results with gold compounds are attained. In one instance aurotherapy saved the life of a patient under my care.

DR. JOSEPH J. ELLER: I treated a patient with lupus erythematosus disseminatus recently. The condition responded favorably after ten daily injections of dextrose solution, with almost complete disappearance of the eruption. The patient was hospitalized.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. I should suggest that the patient be hospitalized and examined for the purpose of detecting a focus of infection. I strongly suspect that in this case tuberculosis may constitute such a factor.

DR. GEORGE M. MACKEE: One never knows what is going to happen in such a condition. Some eruptions of this nature clear up spontaneously; a great many do not. I have found it best to begin treatment with a mild soothing lotion, followed later by lotio alba. I favor hospitalization of the patient, examination and the postponement of aurotherapy. It is particularly important that foci of infection be cleared up.

DR. MAX SCHEER: A number of years ago Ehrmann published statistics of the causes of death in cases of lupus erythematosus acutus disseminatus as shown by observations at autopsy. In about one third of the cases studied, death was apparently due to tuberculosis, and in about two-thirds, to septic infection.

Acute eruptions of lupus erythematosus on the face seem to clear up best after the application of a lotion having a suspension of powder, such as a mild lotio alba or a calamine lotion. This may be due to the fact that the sediment (powder) protects the skin from light.

DR. HOWARD FOX: I realize the grave nature of this type of lupus erythematosus and have seen a great many patients with this condition die, especially as the result of general tuberculosis. It is difficult to give a prognosis in such cases, as the disease is so capricious. I do not think that all cases of lupus erythematosus disseminatus are complicated by tuberculosis. I have not used aurotherapy in this case, but have given the patient injections of bismuth, which were followed by a slight improvement of the condition within three weeks.

REPORT ON A CASE PREVIOUSLY PRESENTED. DR. GEORGE C. ANDREWS.

I should like to report on the case of the baby with an ulcer of the anus, which I presented for diagnosis at the last meeting. The reaction to tuberculin was negative. A roentgenogram of the chest gave normal findings. The inoculation of guinea-pigs did not reveal tubercle bacilli. The child is almost well. A biopsy showed no evidence of tuberculosis. The ulcer has healed under treatment with wet dressings applied alternately with dry heat. The final diagnosis was pyogenic ulcer of the anus.

PHILADELPHIA DERMATOLOGICAL SOCIETY

R. L. GILMAN, M.D., *Secretary*

March 17, 1933

F. D. WEIDMAN, M.D., *President, in the Chair*

ICHTHYOSIS HYSTRIX. Presented by DR. J. P. GUEQUIERRE.

A schoolgirl, aged 17, complains of thickening of the skin of the extremities. The skin is generally somewhat dry and ichthyotic, but the patient perspires freely on the palms and soles. Over both upper and lower extremities there is a dirty grayish hyperkeratosis, which is marked over the extensor surfaces of the ankles, knees and buttocks, where it forms closely set spicules and warty papillary elevations. The margins of the patches are ill defined. The hyperkeratosis is less marked on the extensor surfaces of the wrists and on the dorsa of the hands and elbows, but it is thick enough to accentuate and coarsen the normal lines of the skin. The flexor surfaces of the extremities are relatively free. There are several light areas of relatively normal though dry skin in the midst of the hyperkeratotic fields, which are apparently the sites of recent epithelial denudation. Over the shoulders, down the midline of the spine and in the groins are scattered small fields of mild hyperkeratosis. The scalp is also diffusely involved. There has been no loss of hair.

General physical examination showed nothing significant except obesity and a questionable enlargement of the thyroid gland. The basal metabolic rate was minus 7.

LINEAR NEVUS. Presented by DR. J. P. GUEQUIERRE.

A white girl, aged 16, presents a linear lesion on the right leg, extending irregularly from the base of the great toe to the lower third of the thigh and ranging from 0.5 to 4.5 cm. in width. The eruption consists of a varying amount

of yellowish-green dried encrustation on an erythematous scaly base. This encrustation comes off about once a month and shortly accumulates again. Similar smaller lesions are seen on both elbows. On the right hand the lesions involve all the fingers and the thumb and extend along the index and middle fingers, joining at the web and extending over the dorsal surface of the hand as far as the lower part of the wrist. The fourth and little fingers are involved to a much lesser extent, and the lesions are definitely verrucous. The condition has been present since birth, with no change in the appearance. For the past two years the patient has had ultraviolet and roentgen treatment (the number of exposures is unknown) and has taken potassium iodide by mouth, with no results. The patient's mother has a similar lesion on the fingers of the left hand.

DISCUSSION

DR. F. D. WEIDMAN: Histologically, cases of this type generally prove to be fibrous hyperplasias. The logical procedure would be to treat them as keloids. One of the patients who was presented has been treated by injections of a fibrin ferment. Similar treatment might be tried in this case, if everything else has failed.

DR. ABRAM STRAUSS: I think that the first treatment suggested by Dr. Weidman is better, although there would be a great deal of scarring.

DR. F. D. WEIDMAN: I was impressed by the manner in which one of the fibrous bands extended down the back of the hand and ended in a perfect inverted Y on the fingers. There is some discussion as to the reason for such bandlike or linear configurations, whether they occur as fibrous ridges on the skin, as in the case presented, or as pigmented moles. Is the particular linear arrangement referable to the influence of an underlying nerve trunk or is it a metameric expression? The branching on the fingers points toward the neurologic explanation.

DR. ABRAM STRAUSS: Is there any histologic resemblance between the underlying elements of the skin and the so-called scleroderma?

DR. F. D. WEIDMAN: No, none at all. The tissue in these nevi is of a young fibrous type, whereas in scleroderma the tissue is old and dead. In the early stages of scleroderma the proliferative infiltration of round cells would serve to distinguish the two conditions.

ADENOMA SEBACEUM. Presented by DR. C. S. WRIGHT and DR. O. D. SCHAUL.

A white woman, aged 35, has had an eruption on her face since the age of 9. It has not changed in appearance during the subsequent twenty-six years. She was one of five children; no similar eruption appeared in the other children. She attended school through eight grades and had no difficulty in her studies. There was a history of convulsions during childhood.

Examination showed large numbers of closely grouped papules over the prominent part of the cheeks and on the chin and forehead. Some of the papules were reddish, while others were flesh-colored or waxy; the intervening skin showed numerous telangiectases.

LINEAR SCLERODERMA WITH HEMIATROPHY OF THE FACE. Presented by DR. HERMAN BEERMAN, by permission of Dr. Joseph Stokes, Jr., Pediatrics Department, University Hospital.

A schoolboy, aged 7, who has been sparsely nourished, presents a striking atrophy of the left side of the face which involves not only the external structure but the tongue as well. There are two healing ulcers in the buccal mucosa on the left side. The skin over the left side of the face and forehead is definitely sclerodermatous. In addition both upper extremities are affected; linear bands of scleroderma extend to the fingers, involving particularly the ring and middle fingers of the left hand and the middle finger of the right hand. There is a moderate degree of fixation of the fingers. The left lower extremity is similarly involved, and the second and third toes are bound.

General examination showed slight scoliosis on the left side, a slightly palpable liver and a faint systolic murmur in the mitral area. The blood and urine were normal. No biopsy was performed. Serologic tests of the blood gave negative results.

The patient was well until he was 4 years old, when a lesion in the form of a white band started on the left side of the forehead. In a few months other lesions appeared as linear streaks and spots. Within one year they developed to their present extent. The patient was treated with a fibrin ferment, which apparently arrested the process; there was a slight softening of the lesions. Additional measures consisted of ultraviolet therapy, sweat baths and the application of ointments. Three and a half weeks ago the abrasion of a finger was followed by a furuncle on the back of the right hand, which discharged pus. This has practically healed. There was a rise in temperature to from 99 to 100 F. during the period of inflammation. There were no particularly marked general symptoms associated with the fever. The patient is presented mainly for therapeutic suggestions.

DISCUSSION

DR. F. D. WEIDMAN: Try atropine. A young girl whom I showed twice before this society because of unilateral scleroderma extending from the chest down the arms (A Case of Unilateral Scleroderma with Zosteriform Distribution, ARCH. DERMAT & SYPH. **25**:560 [March] 1932) has undergone marked improvement with this treatment. Atropine was used because it was believed that the process was due to vascular spasm with a neurologic sympathetic basis, and a relaxing effect was desired. Whether improvement was due to the atropine or to the baking and massage is not known.

DR. O. D. SCHAUL: I saw a patient with a similar condition who was in the hospital for six months. She could hardly move the extremities when she was admitted. She was treated with diathermy and other physical therapy. The condition improved markedly, although the eruption was of the generalized type. Dr. Guequierre suggested massage with cod liver oil. This and treatment with infra-red rays gave relief. Pains in the joints were also relieved by diathermy; there were loosening of the skin and a slight increase in muscular motion. The patient was able to walk when she went home, and the condition was much relieved. She received very large doses of thyroid by mouth until her basal metabolic rate reached 100. She was poisoned with thyroid extract, although the preparation may have been partly responsible for her improvement. She gained 13 pounds (5.9 Kg.) and ceased to suffer from indigestion after massage with cod liver oil was given.

DR. ABRAM STRAUSS: I know of cases of generalized scleroderma in which typhoid vaccine was used with good results. I gave it to one of my patients and noticed marked improvement when an intravenous injection was given every third day. There was a rise in temperature to 103 and 105 F. The patient had had the condition nine years when I first saw her, and her jaw was locked. Following treatment with the vaccine alone she left the hospital in fine condition, gained weight and was able to open the mouth and eat normally. Six months later gangrene of the fingers developed, which was relieved by sympathectomy.

DR. D. M. PILLSBURY: Have there been any beneficial results following parathyroidectomy in cases of this type?

NODULO-ULCERATIVE GUMMA OF THE KNEE SIMULATING LUPUS VULGARIS. Presented by DR. C. S. WRIGHT and DR. J. P. GUEQUIERRE.

A white woman, aged 51, had cutaneous lesions on each knee for twenty years. The lesion on the right knee, which measured 3 inches (7.6 cm.) in diameter, was studded with apple jelly nodules the size of a pea. The left knee showed numerous nodules varying in size from that of a pea to that of a hickory nut, a few of which were ulcerated. There was considerable scar formation extending down the upper

third of the leg. There was no pain. The history was negative for syphilis. The Kolmer test gave a reaction of plus 4. A section of tissue taken for histologic examination showed dense fibroblastic proliferation and infiltration of mononuclear cells in the corium. Large monocytes predominated, and there was an occasional Langhans giant cell. Numerous small blood vessels showed evidence of endarteritis.

The patient was treated with iodides by mouth and with luetin subcutaneously, the latter in doses beginning with 0.2 cc., with an increase of 0.1 cc. for each dose. Within five weeks all the nodules vanished, leaving smooth pigmented scars.

DISCUSSION

DR. C. S. WRIGHT: This case was presented for two reasons. In the first place, I have always taught that apple jelly nodules are one of the typical marks of lupus. The nodules were so typical in this patient that a diagnosis of lupus vulgaris was made on the basis of the appearance, but this diagnosis did not explain the large nodules on the left knee. Of course, since the condition cleared up in five weeks, it could not be lupus vulgaris. The pathologist also reported lupus vulgaris.

Secondly, I had prescribed luetin only for the treatment of this patient, but one dose of neoarsphenamine was given against my orders, so that the remarkable improvement cannot be attributed to luetin.

DR. F. D. WEIDMAN: I thought that the condition looked like syphilis. At the same time, in view of the histologic similarity between the lesions of syphilis and those of lupus vulgaris (both consist of epithelioid cells, giant cells and other cells), I can understand how, if the gumma remained small enough, it could present an apple jelly appearance clinically.

DR. G. V. KULCHAR: The patient apparently had large bilateral, nodular, ulcerative lesions involving both knees. I suggest the diagnosis of syphilitic bursopathy of Verneuil for the infiltration now involving the prepatellar bursa of the left side.

DR. D. M. PILLSBURY: I was of the same opinion as Dr. Kulchar, but the patient states that the swelling extended farther down than one would expect in syphilitic bursopathy. Dr. Wright tells me that there was no evidence of swelling of the bursa at the time of the patient's admission to the hospital.

SUBUNGUAL EXOSTOSIS. Presented by DR. L. GRIGGS for DR. J. F. SCHAMBERG.

A white woman, aged 29, presented a tumor 2 cm. in diameter under the nail of the great toe of the right foot, of two months' duration. It was ulcerated. A roentgenogram was taken, and a diagnosis of subungual exostosis was made. The patient was sent to the orthopedic department of the hospital for surgical removal of the growth.

DISCUSSION

DR. D. M. PILLSBURY: Shaffer states that complete surgical removal is the only successful treatment for this condition. The exostosis must be cut all the way down to the phalanx from which it arises.

DR. F. D. WEIDMAN: I should like to suggest the possibility of glomus tumor. Masson has recently pointed out that some subungual tumors are due to small nevic rests which consist of a mixture of angiomatous, muscular and nerve tissue. For a long time histopathologists have been puzzled about certain tumors which have the appearance of fibrosarcomas or, possibly, tumors of nerve sheath cells, which are also spindle cells, together with the angiomatous intermixture. I suggest that the sections be restudied in the light of the glomus tumor of Masson.

CARCINOMA; METASTASES OF THE SKIN. Presented by DR. J. P. GUEQUIERRE.

A man, aged 54, presents a large nodular mass in the left inguinal area, with extension upward on the abdomen. Two hard reddish-purple lesions are present, measuring about 1 inch (2.5 cm.) in diameter. There are several smaller con-

tiguous growths. One lesion is to the left of and just below the umbilicus. The right inguinal region is also involved. Smaller lesions are scattered over the abdomen, chest, thighs and axillae. There is one lesion on the right side of the neck posteriorly.

The average weight of the patient was 137 pounds (62.1 Kg.), but it decreased to 105 pounds (47.6 Kg.) in one year. He first noticed a lump in the left inguinal region about one year ago. This has enlarged slowly and gradually, and new lumps have developed. About six months after the appearance of the lump on the left side the patient noticed lumps developing in the right inguinal region.

The blood count was normal. The patient states that following the last roentgen examination he noticed a reaction in the lesions; they seemed worse. A biopsy was performed, and the lesions were believed to be cutaneous metastases of an internal carcinoma.

DISCUSSION

DR. F. D. WEIDMAN: Microscopically, the lesions are adenocarcinoma, the cells being arranged in the form of tubes with definite lumens. Singularly they contain many pus cells. The possibility that the lesions are primary in the sweat glands seems to be disposed of by the anatomic distribution of the tumors grossly. Only two types of malignant tumors of the interior metastasize to the skin: hypernephromas and melanosarcomas. I suggest that attention be paid to the suprarenal region of this patient. According to his history, he had prolapse of the rectum in childhood; his mother had to reduce the prolapse before he could have a bowel movement. However, according to the roentgenologist, the lower part of the bowel appears to be normal. The preponderance of lesions in the inguinal region suggests an origin in the pelvic parts.

ACRODERMATITIS ATROPHICANS CHRONICUS. Presented by DR. J. V. KLAUDER.

A man, aged 60, from the Philadelphia General Hospital, presents lesions on the legs of twelve years' duration. There was a gradual development of similar lesions on the arms, but these have disappeared. The Wassermann reaction was negative. (Sections were exhibited under the microscope.)

DISCUSSION

DR. F. D. WEIDMAN: I believe that this is a case of porokeratosis of Mibelli. I am aware that in descriptions in textbooks the peripheral infiltrated margin has a median, depressed, annular ditch extending around it; I have not seen any cases described in textbooks in which it is absent; however, in the literature there are cases in which the margin has an infiltrated appearance resembling that in carcinoma and in which the ditch was absent. The histologic sections have disposed of the possibility of epithelioma; there are pathologic changes in the corium. The sections do not show the tuberculoid architecture that is found in porokeratosis, but that may be due to the fact that an unfavorable part of the lesion was selected for biopsy.

DR. C. S. WRIGHT: I spent a year in the study of porokeratosis. I traced the disease through three generations and cut about a thousand sections, which I stained and studied. I cannot detect, from the clinical appearance of the lesions or of the sections in this case, any resemblance to porokeratosis. Some lesions have been reported that do not have the central furrow along the elevated border, but I believe, and I think that Dr. Wise believes, that those were not lesions of porokeratosis but were nevi.

DR. F. D. WEIDMAN: A case may be recalled that was reported by Dr. Corson before the Atlantic Conference (An Unusual Ringed Eruption, ARCH. DERMAT. & SYPH. **18**:415 [Sept.] 1928). Dr. Fred Wise subsequently reminded me of a report in the ARCHIVES of a case of porokeratosis. After looking it up I had to agree that the condition reported by Dr. Corson was porokeratosis. Neither of these cases exhibited the ditch. I saw two cases of porokeratosis in

Birmingham on the same day, in one of which the diagnosis was confirmed histologically. The central ditch was absent in both of these cases, which were also of many years' duration.

DR. D. M. PILLSBURY: There is one rather disconcerting point in the patient's history. He states that he has had similar lesions over the extensor surfaces of the wrists, yet there is no scarring or atrophy evident at the present time.

DR. ABRAM STRAUSS: In spite of the histologic observations, I am inclined to place this case among the precancerous dermatoses described by Jadassohn. The condition has the clinical appearance of Bowen's dermatosis that is seen on the body, with the exception that there has been no breaking down; however, breaking down does not always occur in that condition. The sections may be cut the wrong way and may not show the typical structure.

DR. C. S. WRIGHT: I believe that in taking a biopsy specimen in a case like this it is better to take a small piece from the border, with a little normal skin on each side. I think that Dr. Strauss' point that the sections may not show the typical structure is well taken. Often one has to cut through the whole series in order to get the right picture.

ALOPECIA CONGENITALIS HEREDITARIA VERTICIS. Presented by DR. MORRIS MARKOWITZ.

Brothers, aged 19 months and 5 years, respectively, each present a circumscribed smooth hairless patch 1½ by 2 inches (3.77 by 5 cm.) in size on the vertex of the scalp; these were present at birth. The father and the paternal grandmother of the children had similar congenital lesions also located on the vertex of the scalp.

DISCUSSION

DR. ABRAM STRAUSS: I think that the condition is scleroderma.

DR. F. D. WEIDMAN: In alopecia of congenital nature there should not be changes in the texture of the skin. The fibrosis in one of the lesions is so thick that it feels like a button. There are numerous scarlike depressions; of course, these may be neurotic excoriations superimposed on the alopecia. It is known that favus produces scarring, and pseudopelade is followed by scarring. I do not believe that the condition is alopecia, but with the history available I cannot suggest an alternative diagnosis.

DR. C. S. WRIGHT: I think that the most unusual feature in these cases is the fact that the condition runs through three generations. As I see it, there is a cicatricial condition, with permanent alopecia, but I do not know what name one would give it.

DR. ABRAM STRAUSS: Would these lesions come under the heading of nevi?

DR. H. H. PERLMAN: In pediatric practice one often sees injuries produced by forceps. The condition looks like traumatization rather than alopecia.

LICHEN PLANUS ZOSTERIFORME. Presented by DR. R. L. GILMAN.

A woman, aged 26, from the Women's Medical College and Hospital, presents an eruption of five months' duration. There is no itching. The lesions are flat-topped polygonal papules; the arrangement is roughly that of zoster in the right thoracic region.

DISCUSSION

DR. ABRAM STRAUSS: The lesions are almost disappearing, according to the history. I think that the pigmentation is typical of disappearing lichen planus.

DR. F. D. WEIDMAN: Some of the lesions are markedly translucent. At the same time there is not quite enough hyperemia of some of the other lesions to support the diagnosis of lichen planus zosteriforme. I should suggest lymphangioma circumscriptum, which sometimes occurs in zosteriform distribution.

PAPULONECROTIC TUBERCULID ASSOCIATED WITH ACTIVE TUBERCULOSIS. Presented by DR. L. GRIGGS for DR. S. S. GREENBAUM.

A woman, aged 26, with a history of active pulmonary tuberculosis, presents multiple small bluish infiltrated lesions with necrotic centers, which are distributed about both ankles and the lower part of the legs, of six months' duration. The patient was first treated with intravenous injections of 10 mg. of gold and sodium thiosulphate; a severe reaction followed. She received no treatment after that.

DISCUSSION

DR. ABRAM STRAUSS: It is unusual to see lesions so low and so sharply confined to the lower extremities.

DR. F. D. WEIDMAN: I wonder whether lupus pernio is associated, and whether it has determined the development of the lesions in the affected parts. The patient complains of cold feet.

DR. ABRAM STRAUSS: There is a bluish-red tinge to the skin of the lower extremities. In this type of tuberculosis gold preparations have only a temporary effect.

DR. C. S. WRIGHT: I have not treated many patients with this condition. In the papulonecrotic type of tuberculid gold preparations are not particularly beneficial.

DR. J. M. SCHILDKRAUT: I treated a patient in whom exfoliative dermatitis developed following treatment with a gold preparation.

RECURRENT BULLOUS ERUPTION ON THE PENIS AND SCROTUM DUE TO PHENOLPHTHALEIN. Presented by DR. C. S. WRIGHT and DR. REUBEN FRIEDMAN.

A medical student, aged 22, from Temple University Hospital, took one half of an Ex-Lax tablet ten days ago. One hour later he experienced a tingling and itching sensation in the scrotum and penis. On arising the next morning this sensation was intensified. On examination that afternoon the skin of the genitals was found to be intensely purple; the scrotum was somewhat edematous. In the middle of the anterior aspect of the right thigh, about an inch below the inguinal fold, was a mildly inflammatory, brownish, sharply marginated, smooth, oval patch about the size of a hen's egg. On the following day the patient presented a large bulla containing clear fluid on the dorsum of the penis, which involved the coronal sulcus and the shaft immediately behind it. Numerous small vesicles and blebs were also present on the scrotum, mainly in the vicinity of the median raphe.

This was the fourth attack that the patient had experienced within the last four years. In each instance the eruption followed the ingestion of a phenolphthalein cathartic. The cutaneous involvement in each preceding attack was of the same character as in the present attack and was limited to exactly the same areas on the penis, scrotum and right thigh. Healing in each instance usually took place within two weeks.

BISMUTH PIGMENTATION OF THE BUCCAL MUCOSA; HEALED CARCINOMA AND GUMMA OF THE TONGUE. Presented by DR. C. S. WRIGHT and DR. REUBEN FRIEDMAN.

A white man, aged 50, presented an elongated ulcer approximately 1 by 3 cm. along the left margin of the tongue. The anterior border was elevated and rolled out; it bled easily on traumatization. The posterior two thirds of the ulcer was painless and more punched out; this part did not bleed on traumatization. The Wassermann reaction of the blood was positive. The patient gave a history of a penile lesion thirty-five years previously.

Treatment with insoluble bismuth in oil was instituted. Seven weeks later severe stomatitis caused by bismuth developed, with pigmentation of the tongue and the buccal mucosa. Substitution of neoarsphenamine resulted in a severe

reaction within a few hours. A few intramuscular injections of mercury succinimide produced intense salivation and soreness of the gums. Meanwhile the anterior third of the ulcer continued to spread, and resort was made to roentgen therapy. The tongue healed completely. At present the patient shows pigmentation of the buccal mucosa due to bismuth, involuting mercurial stomatitis and healed gumma and carcinoma of the tongue.

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. Driver, M.D., *Reporter*

Regular Meeting, March 23, 1933

E. W. Netherton, M.D., *Presiding*

Lymphogranuloma Inguinale: Spontaneous Recovery. Presented by Dr. H. F. De Wolf.

E. M., an Indian woman, aged 27, was admitted to the service of Dr. Cole and Dr. Driver at the City Hospital, Cleveland, on March 14, 1933, because of a pyogenic infection of the right thumb with lymphangitis. Healing was uneventful. The patient gave a history of having been operated on in the same hospital in 1928 for a lesion in the left groin which was thought to be a strangulated femoral hernia. At the time of operation infected lymph nodes were found, and healing was slow. The Wassermann and Kline tests of the blood at this time were positive. Examination of the spinal fluid yielded negative results. The Wassermann test of the blood was negative in 1928. Because of the previous history, Frei tests were performed and were found to be strongly positive with three different antigens.

A biopsy specimen removed from one of the nodes in 1928 was reexamined; the section revealed marked edema and infiltration of the glandular tissue and of the periglandular areas with mononuclear and leukocytic cells. There were multiple areas of necrosis in some areas, with obliteration of the normal glandular structure. There were no giant cells.

Lymphogranuloma Inguinale; Esthiomene. Presented by Dr. H. F. De Wolf.

E. S., a Negress, aged 46, was admitted to the service of Dr. Cole and Dr. Driver, at the City Hospital, on Nov. 30, 1932, complaining of ulceration of the vulva. Examination revealed marked swelling of the right labium majus, with a punched-out, irregular ulcer about 0.5 cm. in diameter on the lower right side of the vagina. On a previous admission in 1930, a diagnosis of granuloma inguinale had been made, and improvement had resulted following the use of antimony and potassium tartrate. The lesion had gradually healed following additional therapy with this drug, but the edema had persisted.

The Wassermann test of the blood was negative. Several Frei tests were strongly positive. The smears examined for Donovan's bodies did not reveal these organisms. A specimen taken for biopsy from the edge of the ulcer of the vagina showed that the basal layers of the epidermis were necrotic. There were vacuolated cells which infiltrated the corium and the connective tissue with occasional polymorphonuclear, leukocytic and foreign body giant cells. A pathologic diagnosis of chronic inflammation was made.

Two intravenous injections of fuadin were recently given, but it is too early to note any change in the condition.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

E. R., a Negress, aged 33, was admitted to the service of Dr. Cole and Dr. Driver, at the City Hospital on Jan. 16, 1933, complaining of pain in the lower portion of the back and a tender swelling of the left groin. The patient dated her illness from a fall on Dec. 25, 1932. The mass in the groin had increased slowly in size. There were slight malaise, night sweats, slight loss of weight and a low grade fever. Examination revealed a hard mass in the left groin, lying above Poupart's ligament and measuring about 6 by 7 cm. There was no lesion on the genitalia. Several Frei tests were strongly positive. The Wassermann test of the blood was negative.

It is too early to report results of therapy.

SERONEGATIVE PRIMARY SYPHILIS AND LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

N. S., a Negro, aged 24, from the service of Dr. Cole and Dr. Driver, had been treated in the outpatient department of the City Hospital since December, 1932, for seronegative primary syphilis. On Feb. 12, 1933, he was admitted to the hospital because of bilateral inguinal adenitis.

Examination revealed a large, indurated mass, about the size of a hen's egg, in the right groin, with a draining sinus from the center of the lesion, lying above Poupart's ligament and a somewhat smaller swelling with a draining sinus in the left groin, lying slightly below Poupart's ligament.

The Wassermann and Kline tests of the blood have remained negative. Several Frei tests have been strongly positive since the patient's admission to the hospital. There has been slight improvement following the administration of filtered doses of roentgen rays. Forty cubic centimeters of fuadin has been given intravenously in addition to the usual routine treatment for syphilis. Slight improvement has resulted.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

W. W., a Negro, aged 17, was admitted to the service of Dr. Cole and Dr. Driver at the City Hospital on March 13, 1933. Following multiple exposures prior to admission a tender mass almost the size of a lemon had developed in the left groin. The center of the lesion was fluctuant, and several cubic centimeters of pus was aspirated. At the time of admission there was a superficial ulceration about 1 cm. in diameter on the glans penis near the meatus. The patient complained of malaise, headache, chills and fever.

The Wassermann test of the blood was negative. The Frei test was positive with three different antigens.

Treatment has consisted of rest in bed. The bubo has been aspirated three times. There has been no appreciable change in the patient's condition.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

W. R., a Negro, aged 35, was admitted to the service of Dr. Cole and Dr. Driver at the City Hospital on Feb. 7, 1933, complaining of a swelling in the right inguinal region which had started about January 10 and was associated with malaise and slight loss of weight. The patient gave a history of having contracted syphilis fifteen years previously and of having received treatment over a period of several years. He said that he had not had extramarital exposures.

Examination revealed a painless, oval, indurated mass in the right groin about 5 by 6 cm. in diameter. At the outer border of the lesion was a small, draining sinus. No lesion was found on the genitalia.

The Wassermann test of the blood was negative. Examination of the spinal fluid yielded negative results. The Frei test was positive with two different antigens. The patient has had a temperature of approximately 38 C. (100.4 F.)

since admission. Treatment has consisted of intravenous injections of a total of 60 cc. of a 1 per cent solution of antimony and potassium tartrate. No improvement has been noted.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

D. T., a Negro, aged 27, from the service of Dr. Cole and Dr. Driver at the City Hospital, had gonorrhea and syphilis in 1923, followed by treatment for three weeks. In 1930 the patient had a penile lesion and a urethral discharge which he treated himself. On Feb. 19, 1933, he noticed that a swelling was developing in the groins. The last sexual exposure had been on February 3. The patient complained of headache, chills and malaise.

Examination revealed an indurated, firm, slightly tender mass in each groin. In the right groin the lesion was about the size of a small lemon, and in the left groin, somewhat smaller. On admission to the hospital, the patient's temperature was 38.8 C. (101.8 F.). There were no sinuses and no fluctuating areas. The Wassermann test of the blood was negative. The Frei test was positive on two occasions.

The patient has been given no therapy except rest in bed. The temperature became normal at the end of seven days, and the constitutional symptoms subsided. The mass in the left groin diminished considerably in size and is no longer tender.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

M. C., a Negro, aged 25, was admitted to the service of Dr. Cole and Dr. Driver at the City Hospital on Jan. 18, 1933, for treatment of seropositive primary syphilis with a positive reaction to dark-field examination from a lesion on the glans penis. Treatment with aminohydroxyphenyl arsenoxide was instituted, and the primary lesion disappeared, although during the last week of February a swelling developed in the groins, gradually becoming larger and producing large bilateral lesions with a matting together of the nodes, which were quite tender. On the left side there was a fluctuating area. In addition, the iliac glands on both sides were much enlarged and slightly tender.

The Wassermann test of the blood became negative. The Frei test was strongly positive on two occasions.

Treatment has consisted in the aspiration of pus from the left side and rest in bed. The temperature has fluctuated between 38 and 39 C. (100.4 and 102.2 F.). The buboes have increased in size.

DISCUSSION

DR. H. N. COLE: We have purposely presented this group of cases of lymphogranuloma inguinale to illustrate what we think is a rather common disease. No effort has been made to collect the group of cases; they are simply the routine patients coming to the hospital with dermatologic cases, cases of syphilis and other conditions. Moreover, the group is interesting in itself, as it illustrates the different phases of the disease. In one of the patients there was a glairy mucous discharge from the urethra for a few days. An examination of the interior of the urethra revealed, just inside the lip, a small ulceration the size of a pinhead, the primary lesion. Three of the patients illustrate well the premonitory symptoms that are present in the disease. One of them complained of night sweats, chills, headache and malaise. Occasionally the symptoms are severe. In one of the patients there was a generalized grouped eruption resembling somewhat cutaneous lesions that have been described in lymphogranuloma inguinale. There are reports of erythema nodosum, erythema multiforme, erythema scarlatiniforme and urticarial eruptions as complications of the disease. In two of the patients there was a persistent high temperature. The fever in this disease may be either intermittent or remittent, and, as shown in the temperature charts of the patients, it may rise even to 39 or 40 C. (102.2 or 104 F.). One of the patients was afebrile. The Indian patient presented

gives an interesting history. She was a patient in this hospital in 1928 for what was considered to be a strangulated hernia. At the time of operation, a mass of inflamed lymph nodes was found; these were excised, and the area healed slowly. Dr. De Wolf went to the department of pathology, examined the slides and found that they show the typical picture of lymphogranuloma inguinale. Moreover, the patient had a positive Frei reaction. The final patient of whom I wish to speak is the one with the extensive elephantiasis of the vulva and an ulceration in the posterior commissure. This is probably a mild example, perhaps a beginning stage of a later esthiomene. The elephantiasis that we find in this patient is not due to lymph stasis, but, as Barthels and Liberstein have shown, is a typical reaction of lymphogranuloma inguinale: obstruction of the lymph channels with specific tissue. As would be expected, the patient has a positive Frei reaction. I feel that this is an interesting group of cases of lymphogranuloma inguinale, and that if other clinics in this country take the trouble to study patients suffering from adenitis, especially of the inguinal glands, they will find that a generous proportion of them are suffering from this disease.

Dr. H. F. De Wolf: The patient who now shows a definite lymphogranuloma inguinale was in the City Hospital in 1930 with a condition diagnosed as granuloma inguinale; I believe that there may be some question about the earlier diagnosis. It has not been possible to reexamine the slides for Donovan's bodies. Also, one would expect the patient to have had a recurrence of granuloma inguinale with the amount of treatment with antimony and potassium tartrate that she received at that time. However, the fact that the patient now has lymphogranuloma inguinale is unquestioned. I should like to report the case of a patient whom I saw recently. He had a scar in the groin and gave a history that in 1903 he had been operated on at the Lakeside Hospital for an "acute inflammation" of the inguinal lymph glands. I performed a Frei test recently and found it to be strongly positive. It is my opinion that the man had lymphogranuloma inguinale, and that this is fairly good evidence of the existence of this disease in Cleveland thirty years ago.

Dr. E. W. Netherton: I have seen two patients who presented an unusual type of elephantiasis involving the penis and the scrotum which developed suddenly after intercourse in syphilitic patients who had neurologic findings. Cases of this type have been described in MacLeod's textbook. I wonder whether Dr. Cole considers that these cases are possibly due to lymphogranuloma inguinale?

Dr. H. N. Cole: I am not familiar with the condition of which Dr. Netherton speaks.

Dr. E. W. Netherton: In one of the cases shown there was an unusually severe Frei reaction. Is this type of reaction unusual?

Dr. J. V. Van Cleve: The reaction to the Frei test varies somewhat in different cases. It has been our experience that in cases with bilateral involvement the reaction is more severe than in those with unilateral involvement. We also find that in early cases the reaction may be light at the start and become stronger as the disease progresses.

Scleroderma with Atrophy. Presented by Dr. E. W. Netherton.

M. S., a white girl, aged 16, six years prior to admission had suffered from an attack of sore throat accompanied by high fever. Shortly afterward, several white spots appeared on the trunk. These have become gradually larger and have assumed a brownish-red, atrophic appearance. Within the past few months two new, dime-sized areas, ivory white, sclerotic, smooth and shiny, with a faint red areola, have appeared on the chest. Over the back there are five areas approximately palm-sized, which are well demarcated, showing definite atrophy. Friction produces an erythema at the margin of the lesions. The family history is irrelevant. The patient has had the usual diseases of childhood; following tonsillitis, the tonsils were removed at the age of 6. General physical examination revealed nothing

abnormal. The Wassermann test of the blood was negative. The blood count and differential test were normal.

The patient has received tonic measures and small doses of thyroid extract.

DISCUSSION

DR. H. N. COLE: I agree with the diagnosis in this case. About three years ago I saw a patient with a condition similar to this, which had followed a ruptured appendix. I should suggest that a basal metabolism test be performed in this case.

DR. H. J. PARKHURST: I agree with the diagnosis. The more recent lesions on the chest are typical. However, I feel that the lesions on the back might easily be mistaken for lipodystrophy such as described by Gilchrist.

GRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

L. C., a Negro, aged 32, from the service of Dr. Cole and Dr. Driver, was admitted to the City Hospital on March 21, 1933, complaining of swelling and ulceration in the right groin. The disease had been present for approximately five years, and in 1930, the patient received twelve injections of a 1 per cent solution of antimony and potassium tartrate. The lesion had completely healed but had recurred in the scarred area approximately five weeks prior to admission to the hospital.

Examination revealed a large healed scar in the right groin 8 inches (20.3 cm.) in length and from ½ to 2½ inches (1.27 to 6.27 cm.) in width, which had broken down in several areas, showing granulomatous elevations of a dull red color. The scarred area in the groin was continuous with an indurated scar extending downward in the groin onto the right buttock. Granulomatous ulcers similar to those in the groin were present also on the buttock.

The Wassermann test of the blood was negative. The Frei test was strongly positive with two antigens. The blood count and the differential blood count were normal. Tissue smears from the ulcers showed many typical Donovan bodies.

No treatment has been instituted to date.

DISCUSSION

DR. H. N. COLE: This patient presents a typical case of granuloma inguinale. The slide presented clearly shows the presence of Donovan's bodies. It is interesting to compare this case with the cases of lymphogranuloma inguinale also presented today. Here we find the skin diseased, with no glandular involvement.

DR. H. F. DE WOLF: It is interesting to note that in this patient the Frei reaction was positive. We have not had an opportunity to study enough cases of granuloma inguinale with the Frei reaction to know whether it has any significance or not. I am of the opinion, however, that the patient probably has also had lymphogranuloma inguinale sometime in the past.

DR. E. W. NETHERTON: What percentage of recoveries do you have in cases of granuloma inguinale?

DR. H. F. DE WOLF: In my experience, unless the patients are being continuously treated with antimony and potassium tartrate over a long period of time after the lesions have completely healed, they are apt to have a recurrence.

DERMATITIS MEDICAMENTOSA (BISMUTH). Presented by DR. H. F. DE WOLF.

H. E., a white man, aged 30, from the service of Dr. Cole and Dr. Driver, has received since May 10, 1932, continuous treatment for seropositive primary syphilis. Since Jan. 17, 1933, the patient has received a course of bismuth salicylate in oil, consisting of eight weekly injections of 0.26 Gm. each. On February 7, an erythematous eruption appeared on the thighs; it was diagnosed as erythema

multiforme. The eruption improved temporarily following the administration of sodium salicylate. Within a few days, however, the eruption became much more severe and by extension involved also the trunk and arms, without involvement, however, of the face and neck. The lesions consist of bright red maculopapules of various sizes. Associated with these are a rather severe dermatitis which is most marked on the dorsa of the hands, while over the trunk the dermatitis has become dry and scaly, owing to involution. There are no lesions on the mucous membranes.

The patient has been treated with baths of potassium permanganate, injections of sodium thiosulphate and emollients locally.

DISCUSSION

DR. H. J. PARKHURST: My first impression on seeing the patient was that he had an atypical type of pityriasis rosea. On further examination, the papular lesions were rather deeply infiltrated and suggested a syphiloderm, although I realize that with the negative Wassermann reaction this could not be the diagnosis. The patient has considerable seborrhoea capitis, which might explain certain follicular elements in the eruption. On examination of the soles, I found pinhead-sized vesicles suggestive of dermatophytosis. I realize, however, that the desquamating eruption and, in fact, the entire picture could possibly be explained as a dermatitis due to the administration of a heavy metal, arsenic or bismuth.

DR. H. N. COLE: I saw the patient several days ago, and my first impression was that the condition was pityriasis or atypical psoriasis. Neither of the diagnoses, however, to my mind explained the bright red, papular lesions. I then thought that the eruption probably was due to bismuth. The injections of bismuth were then stopped for a while; when they were resumed, the eruption became worse. I think that the condition is an exfoliating type of dermatitis following the administration of bismuth.

DR. E. W. NETHERTON: I have seen patients with similar cases and agree with the diagnosis of dermatitis due to medication with bismuth.

DR. J. R. DRIVER: There are certain features of the papular lesions that suggest somewhat a lichen planus. A biopsy would help to confirm or rule out this possibility. In the French literature lichen planus following dermatitis due to the administration of a heavy metal has frequently been described.

DERMATITIS VENENATA DUE TO MATCHES. Presented by DR. H. F. DE WOLF.

J. M., a white youth, aged 18, from the service of Dr. Cole and Dr. Driver, was admitted to the City Hospital on March 17, 1933, complaining of an eruption on the anterior surface of the right thigh and on the face and the region of the left breast, of two weeks' duration.

Examination revealed a subacute dermatitis on the anterolateral aspect of the upper third region of the thigh, with a similar process of less severity on the face and below the left nipple. The patient stated that for more than two years he had been in the habit of carrying ordinary kitchen matches loose in his right trouser pocket and in the left-hand pocket of his shirt.

Patch tests were performed with a mixture of match-heads made into a paste with water, and tests were applied on the left thigh and on the wall of the right side of the chest. A vesicular dermatitis developed on these areas within twenty-four hours. Control patch tests in which the same materials were used were performed on two other patients, with negative results.

DISCUSSION

DR. HENRY SHAW: The case is identical with one which my associates and I had recently at Lakeside Hospital. Patch tests were positive with the common kitchen matches, while similar tests with safety matches were negative.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *Secretary*

Regular Meeting, March 28, 1933

GEORGE M. MACKEE, M.D., *President*

CUTANEOUS CALCINOSIS. Presented by DR. HOWARD FOX.

Miss N. D., a secretary, aged 39, first noticed the eruption six years ago. It consists of the gradual development of subcutaneous nodules in the vicinity of the numerous joints of the extremities. The lesions are hard, slightly tender masses incorporated with the skin and slightly movable on the deeper parts, and they vary in size from that of a lentil to that of a hazelnut. Roentgen examination showed calcified irregular bodies in the regions mentioned. Histologic examination showed an encapsulated mass, stained deeply and irregularly by hematoxylin. The blood calcium was 17.5 mg. There was a moderate leukopenia, the hemoglobin and red cells being within normal limits. The patient is of average size and apparently is in good general health.

DISCUSSION

DR. H. H. WHITEHOUSE: I should like to know how Dr. Fox is going to treat the condition.

DR. E. R. MALONEY: I agree with the diagnosis. The condition looks very much like one of our cases the report of which we published. I saw a slide of a section taken from one of the tumors which had been stained with silver nitrate, and it showed the characteristic picture; the difference in this case is that the particles of calcium are rather diffused, whereas in our case the calcium was in quite large masses.

DR. EUGENE F. TRAUB: Dr. Fox may be interested to know that at the present time there is a case in the surgical division at Bellevue Hospital, in the service of Dr. Patterson. In this case the lesions are so dense and so deep in the tissues that the limbs are stony hard, and on roentgen examination the soft tissues are seen to be full of streaks and branching filaments of calcium deposit.

DR. E. R. MALONEY: My impression is that there is a pathologic parathyroid element in these cases.

DR. M. J. COSTELLO (by invitation): I believe that this case of cutaneous calcinosis is almost an exact counterpart of the one reported by Dr. Maloney and Dr. Bloom. It differs, however, in that in this patient the blood calcium is 17.5 mg. per hundred cubic centimeters of blood, whereas in their case it was normal. Raynaud's phenomenon in this case is an outstanding feature, and the roentgenograms are interesting and confirmatory; in addition to the calcified nodes, there is early and dense calcification of the costal cartilage. The patient has a subnormal temperature and requires six blankets to keep warm, even during the summer months. An autopsy performed on the patient's mother showed marked atheromatous changes of the arterial blood vessels and atheromatous plaques in the myocardium, on the heart valves and in the aorta.

A CASE FOR DIAGNOSIS (TUBERCULOSIS, SYPHILIS OR AN ERUPTION DUE TO A DRUG?). Presented by DR. R. H. RULISON.

A printer, aged 34, who had not worked for some time, was first seen in the outpatient department for cutaneous diseases of the New York Hospital on March 9, 1933.

His history included a gonococcic infection with testicular involvement about fifteen years previously. He had been married for two years. His wife had had one miscarriage; he stated that she was in good health. In September, 1931, a sore developed on the shaft of the penis. A clinical diagnosis of primary syphilis was made, and treatment was begun without laboratory tests. The lesion healed, and no secondary involvement was noticed. During the remainder of that year he received twelve injections of neoarsphenamine and nine of bismuth tartrate. In the early part of 1932 he was given five injections of neoarsphenamine and six of bismuth solution. A second course of treatment consisted of arsphenamine, and of twelve injections of bismuth solution given later in 1932. Wassermann tests taken after the first course of treatment and six or seven tests taken since have been negative.

In November, 1932, while he was taking a second course of treatment, pain developed in both tibiae, in the lower third region. Slight swelling developed, and tenderness was present. No cutaneous changes occurred over the tibiae. Shortly after this, a dry, red, slightly scaly lesion, the size of a finger-nail, appeared on the shaft of the penis, but not at the site of the first genital lesion. The lesion afterward spread to involve a large part of the shaft of the penis. The eruption was red and shiny; it bled easily on slight trauma and was accompanied by edema resulting in phimosis. Within a few days after the development of the penile lesion, a number of discrete inflammatory lesions appeared on the face, and, more recently, one on the frontal area of the scalp. As presented, the lesions were dollar-sized and sometimes edematous; they were crusted but did not present a constant appearance. At one time after admission to the ward there was a considerable resemblance to lupus erythematosus; at other times the lesions suggested an eruption due to a drug. Urinary tests for bromides gave negative results.

The patient has been treated by several physicians without improvement, and at one time he spent two weeks in the Stuyvesant Square Hospital; during this period the swelling of the tibiae diminished. Otherwise there was no change. Dark-field examination for spirochetes gave negative results.

Two Wassermann tests after admission and a lumbar puncture were negative. The Kline diagnostic test on all the specimens was 4 plus. Hairs from the beard failed to show fungi. Tests with old tuberculin were positive in dilutions of 1:1,000 and 1:10,000. The blood count was essentially normal. Roentgenograms of the sinuses, chest and other parts revealed essentially normal conditions. Roentgenograms of the tibiae showed slight thickening of the anterior cortices, most marked on the right side. Dr. Carty reported that he does not think that the condition is due to a syphilitic involvement. A biopsy specimen was taken from one of the lesions on the head. Dr. Fraser will report his observations.

DISCUSSION

DR. FRED WISE: The clinical picture is that of an eruption due to bromide or iodide salts. A bacteriologic examination of the secretions from the lesions may lead to interesting findings, if an eruption due to a drug can be definitely excluded.

DR. W. J. HIGHMAN: In addition to Dr. Wise's suggestion, I suggest that pemphigus be borne in mind. The lesions remind me of the individual lesions in Eller's case of poisoning by iodide. In Eller's case, at autopsy, iodides were found in the gastric mucosa. I suggest that a gastric lavage be done in this case and that the recovered fluid be examined for iodides.

DR. HOWARD FOX: I agree that the condition looks more like an eruption due to bromide or to iodide than like anything else.

DR. H. H. WHITEHOUSE: I should regard the case clinically as one of iododerma. The patient must have been taking bromide or iodide, although he says that he has not. It is possible that he obtained the drug from some article in his diet.

DR. R. H. RULISON: We shall continue the study of the patient. The eruption on the face is quite different from that of a few days ago; it is sometimes moist and sometimes dry.

SOLID EDEMA OF THE EARS AND FACE. Presented by DR. HOWARD FOX.

Mrs. C. W., aged 42, was previously presented before the Society on Jan. 23, 1933. Since then she has received one treatment with radium in the external auditory canals and fractional doses of roentgen rays to the face and ears at weekly intervals. Ten days before this presentation there was an acute exacerbation, the left ear being swollen and edematous and the external auditory canal occluded. The skin of the left side of the face is sore to the touch and a dusky red. There is no elevation in temperature.

DISCUSSION

DR. PAUL E. BECHET: This is an interesting case, particularly in view of the difficulty of determining the etiologic factors.

DR. HOWARD FOX: I am pleased that a study of the case by a diagnostic group at Mount Sinai Hospital resulted in an opinion which coincides with mine. The roentgen treatment will be continued.

A CASE FOR DIAGNOSIS (CALCIFIED MILIA?). Presented by DR. EUGENE F. TRAUB.

A teacher, a woman, aged 38, born in the United States, presents an eruption which is distributed over the center of the face. Five years ago she had a series of thirteen roentgen exposures for a condition apparently diagnosed as acne but which must have been an exceedingly mild case, as the patient says that at no time did she have active pustules, only lesions resembling those now present. She further states that following each roentgen treatment the skin peeled off. It is difficult to interpret exactly what did happen, as the physician who treated her states that she received one-fourth skin unit each of unfiltered doses. At the same time she was using a lotion, which may possibly have had something to do with the desquamation that followed the treatments. One and one-half years ago another physician treated these marks with an electric needle, and some of the lesions disappeared.

A section was removed for diagnosis, but it was so small that when it was embedded it was found to be too hard to be cut satisfactorily. Another specimen was taken from the center of a small lesion and submitted to Dr. Satenstein, who reported that only two of the sections showed pathologic changes and these were most marked in section 6. In slide 7 a change was just indicated. There was no evidence of sequelae of radiation, basophilic degeneration, telangiectasis or change in the epithelial tissue. There was some sclerosis of the upper cutis (collagen bundles). In the slides indicated, one noticed from without inward that there were indentations extending about half way down the epidermis; they were fairly roundish, margined by a granular layer and filled with a loose, horny substance. Aside from this there was little pathologic change. The elastic tissue was undisturbed. The lesions suggested milium bodies; there was nothing to suggest benign cystic epithelioma.

DISCUSSION

DR. HOWARD FOX: It looks as though the patient has had a number of sebaceous cysts which have become calcified; that seems the most likely diagnosis.

DR. R. H. RULISON: That is my impression.

DR. F. C. COMBES: I agree partly with Dr. Fox. I disagree with him on the question of calcification. My interpretation of this case is that the lesions are keloidal sebaceous cysts. The patient probably had acne, and this was a natural coexisting condition.

DR. J. F. FRASER: The condition may be one of calcification of sebaceous cysts, but the slide does not show it. More sections should be made.

DR. J. H. SCHWARTZ: The microscopic picture is that of keloid. I should make that diagnosis.

DR. FRED WISE: My impression was the same as that of Dr. Fox, that these are small sebaceous cysts which have become calcified. I also think that the patient had considerable acne at one time but is not aware of it now. There is evidence of acne; it is often associated with deep-seated cysts. I think that the change in these bodies is the same as that sometimes seen in milium. I should suggest a second biopsy, one entire lesion being removed.

DR. W. J. HIGHMAN: The calcification that takes place in milium is in the contents of the milium, which acts as a foreign body. But that is not what obtains in the lesion in this case. So far as can be seen, I do not get the impression that this is calcification clinically. The only way to determine the matter is as Dr. Wise has said.

DR. E. R. MALONEY: I agree with those who think that the condition is keloidal. I think that in her youth the woman had acne or sebaceous cysts which were interfered with in some way, and that multiple small keloids have since developed.

DR. GEORGE M. MACKEE: My interpretation is the same as Dr. Maloney's. I think that the woman had acne vulgaris and sebaceous cysts, followed by keloids.

DR. EUGENE F. TRAUB: My first impression, of course, was that the patient had had acne and that she still had a number of tiny sebaceous lesions that had become fibrotic or calcified. I opened a number of them, thinking that I might be able to express some material from the center of the lesion and thus promote healing. All of the lesions, however, were absolutely solid, consisting of an exceedingly tough, dense tissue. This surprised me, particularly as I should not have expected such a lesion to respond to electrolysis or to roentgen therapy. The question as to whether the condition might not be multiple benign cystic epithelioma was apparently settled by the negative report on this section.

DR. FRED WISE: If the lesions are stony hard so that they cannot be cut, what can they be except calcified tissue?

DR. GEORGE M. MACKEE: The fact that the lesions did not improve as a result of roentgen treatment is a point against keloid, as Dr. Traub stated. However, roentgen rays often fail to influence keloids favorably; also, the keloids may have developed subsequent to roentgen treatment.

SUBSEQUENT NOTE.—A subsequent report confirmed the histologic diagnosis of calcified miliary bodies.

A CASE FOR DIAGNOSIS (KELOID OR HYPERTROPHIC SCAR?). Presented by DR. FRED WISE.

On March 11, 1933, a girl, aged 14 years, first applied for treatment at the clinic for skin diseases of the New York Post-Graduate Medical School and Hospital. Her general health is normal. On the extensor surface of the midarea of the left forearm is a lesion said to be of five months' duration. It is approximately 1 inch (2.5 cm.) long and ¾ inch (2 cm.) wide, roughly oval and dusky red, with a smooth, nonscaling surface and sharply defined edges. The patient states that five months ago she noticed a "pimple" which rapidly enlarged, becoming a ring, and gradually cleared in its central portion. This was treated with a strong salve which caused an exudation at the side of the ringed lesion. After the dermatitis had healed, a flat, rather soft, dusky red, plaquelike area remained. There were no subjective symptoms. Histologic examination revealed an area in the corium entirely devoid of elastic tissue. Dr. Satenstein interpreted the changes as those of an organized granulation tissue, secondary to some preceding process of unknown origin.

DISCUSSION

DR. F. C. COMBES: I do not see how one can be expected to make a definite clinical diagnosis. On observation, the lesion looks as much like an early keloid as like anything else. What the original lesion was it is impossible to say.

DR. J. F. FRASER: It looks like a keloid under the microscope.

DR. W. J. HIGHMAN: It is a keloid.

DR. EUGENE F. TRAUB: Dr. Combes expressed the opinion that the lesions in this case clinically resemble keloids. I disagree, because on close inspection dilated hair follicles and more or less normal-looking epidermis may be seen covering the patch. Such an appearance is not found in a true keloid. Though I realize that a diagnosis of sarcoid has been ruled out on microscopic examination, I think that the clinical appearance is that of sarcoid.

DR. HOWARD FOX: I agree with the diagnosis of keloid.

DR. FRED WISE: The fact that the microscope showed the structure of a keloid seems to settle the diagnosis, but I do not think that the lesion looks like keloid clinically.

DR. GEORGE M. MACKEE: I have seen rapidly growing keloids that are discoid, fairly soft at first and red. In such instances the diagnosis is difficult until the keloid has become organized. My diagnosis of this condition is probable keloid.

SYRINGOMA OF THE CHEST AND ABDOMEN. Presented by DR. FRED WISE for DR. LOUIS CHARGIN.

A colored woman, aged 23, was referred by Dr. Chargin to the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital this morning. Her general health is normal, but she says that she has given a positive reaction to the Wassermann test.

On the upper portion of the chest, the epigastric region, the abdomen and the upper extremities are several hundred oval, dark brown, smooth, slightly elevated, soft papules, varying in size from that of a large pinhead to that of barleycorn, and free from scales or other superficial markings. The papules are rather regularly disseminated on the regions mentioned on the trunk, but only a few widely scattered papules appear on the arms and the forearms. The duration of the eruption is said to be two years. With the exception of occasional slight itching, there are no subjective symptoms.

DISCUSSION

DR. HOWARD FOX: There can be no doubt concerning the diagnosis in this case. As to treatment, I should like to mention a case in which I treated one side of the body with about a dozen fractional doses of roentgen rays at weekly intervals. A complete involution of the lesions treated followed.

DR. H. H. WHITEHOUSE: I agree with the diagnosis.

DR. W. J. HIGHMAN: I am in accord with Dr. Wise concerning the diagnosis.

BLUE NEVUS (?). Presented by DR. EUGENE F. TRAUB.

A Russian Jewess, aged 42, states that she has had a lesion on the right cheek since childhood, and that a similar lesion has been present above the left eyebrow for about one year. The lesions are practically flat and level with the surface of the skin; only the older lesion on the cheek shows the slightest elevation. The deep bluish-black color of both lesions seems to be due to a reflected pigment from the depth of the skin, as the skin on the surface appears to be devoid of color.

Both marks are rounded and sharply demarcated and measure only from 3 to 6 mm. in diameter. On the neck are numerous molluscoid nevi which have also been present for about one year. The patient has dermatitis on the face, neck and arms, and to a less degree on the upper part of the trunk. It is for dermatitis that she has come to the clinic.

DISCUSSION

DR. R. H. RULISON: I should call the condition a melanoma.

DR. FRED WISE: Dr. Traub asked whether or not we think that the patient has blue nevi. I have seen two or three instances in which the lesions were so strikingly blue that they gave the impression that something of a bright blue color had been tattooed into the skin; I therefore do not think that these lesions are blue nevi. Bloch stated that on the basis of his staining reaction the cells of the blue nevus and of the mongolian spot are apparently identical and consist of melanoblasts of mesodermal derivation. These cells may give rise to true melanosarcomas, whereas the cells of ectodermal derivation give rise to melanocarcinomas.

DR. GEORGE M. MACKEE: My impression is the same as that of Dr. Wise. I have seen two or three cases presented as blue nevus, and, as Dr. Wise said, the color was a pure blue of striking appearance. These lesions are bluish, but they also contain brown or black pigment, like what we call blue-black moles. I think that the patient is free from danger at present and probably always will be, because the lesions are not likely to be irritated. However, there is potential danger; if I had the lesion I should have it properly excised.

DR. EUGENE F. TRAUB: Several months ago I presented a girl with a similar lesion, which was diagnosed at the Academy of Medicine as a blue nevus. The case was not brought up for discussion, but there seemed to be no question as to the diagnosis. As I have seen three such cases in the past two months, and as the exact differentiation between a blue nevus and a slate-black mole is not entirely clear in my mind, I presented this patient for a discussion on this point. Dr. Wise quoted Bloch on the similarity of the type of melanoblasts in the mongolian pigment spots and the blue nevus. There are some differences, however, in the clinical course of the two lesions, as the mongolian spot usually disappears in the first few years of life, and I know of no instance on record in which a mongolian spot gave rise to a sarcoma. On the other hand, some believe that blue nevi frequently become malignant, a point which is disputed by Becker and others. If the theories of Bloch are accepted, the slate-black mole becomes a melanocarcinoma or a nevocarcinoma, whereas the blue mole, if it undergoes malignant change, becomes a nevosarcoma. Bloch seemed to assume that the slate-black mole is really a malignant condition from the start, and that from the standpoint of possible malignancy the soft brown, nonelevated mole is the most dangerous lesion. This assumption, however, I believe, is not universally held; but, on the other hand, I agree that the soft brown, nonelevated moles may become malignant as readily as the slate-black moles. I believe, with others, that it is not so much the type of lesion as it is the location at points of friction or irritation that determines whether or not the lesion will become malignant. This is particularly true of the flat brown moles located on the hands or feet.

DR. W. J. HIGHMAN: The great difficulty is that we see malignant lesions late and have to try to restore the picture of the cause from that of the effect.

DR. EUGENE F. TRAUB: The color of the blue nevus is due to the deeply lying melanoblasts, which are presumably located two thirds of the way into the true skin. Because of the varying thickness of the overlying layers of derma and epidermis, the color of the marks may differ. Sometimes they are extremely blue, and at other times they may be blue, blue-black, brownish blue or brownish black.

DISCOID LUPUS ERYTHEMATOSUS, WITH GENERALIZED ERYTHEMA (DISSEMINATED LUPUS ERYTHEMATOSUS OR TOXIC ERYTHEMA FROM GOLD?). Presented by DR. H. J. SCHWARTZ.

A Swede, aged 52, was first seen at the New York Hospital on Nov. 2, 1932, complaining of an eruption on the face of five years' duration, beginning on the right cheek and gradually spreading. Physical examination gave negative findings except for hypertrophied tonsils.

From that time until the first of March, 1933, the patient was given sixteen weekly intravenous injections of gold sodium thiosulphate; the first two doses were 25 mg., and the balance, 50 mg. He improved under the treatment, but on March 8 he appeared at the hospital with a generalized macular erythema which he stated had begun a month previously and had spread gradually. There were some scaling and whitish, adherent plaques. There was moderate itching, but there were no constitutional symptoms and no hyperkeratosis of the palms or soles.

The injections of the gold compound were discontinued, and injections of sodium thiosulphate were begun; five doses have been given to date. Patch tests were made on March 22, 10 and 30 per cent gold sodium thiosulphate being used. The reactions (erythema and vesiculation) did not differ from those obtained in controls, so no conclusions could be drawn. A test was made for gold in the tissue, with negative results.

There are now typical pustules of discoid lupus erythematosus on the cheeks, nose and ears and on the right side of the upper lip.

A small piece of tissue from an erythematosquamous patch on the back was removed for histologic study. Dr. Fraser reported the presence of hyperkeratosis, horny plugs dipping into the follicular openings, edema of the epidermis and a modernately inflammatory process confined to the papillary layer and strongly suggestive of lupus erythematosus.

DISCUSSION

DR. W. J. HIGHMAN: This is a difficult case to construe. There is no question that the patient has discoid lupus erythematosus. The interpretation of the more or less generalized eruption on the body is another matter. I should say that a toxic dermatitis arising from treatment with a heavy metal or similar agent ought to be more diffuse. The farther away one walks from the patient, the better one sees that the eruption consists of clusters of small discoid lesions. I, too, have the impression that the condition is a disseminated lupus erythematosus—probably disseminated by the effect of therapy. It is possibly due to the effect of the gold on the pathogen in the discoid lesions and is to be regarded as the product of mobilization of the pathogenic agent, which had been fixed in the old lesions and has been liberated by the gold. If that is true, the significance of the tests comes under scrutiny. For patch tests, I think that the concentration of the testing agent used was very high. Thus the result is not an allergic reaction so much as an irritative one. Moreover, the patch tests may have the same significance as the discoid lupus erythematosus lesion and may have exacerbated the process.

I may not have made myself clear, but there are all kinds of pitfalls to be avoided before we conclude that these so-called patch tests indicate that a patient was poisoned by a medicament.

DR. J. F. FRASER: I agree with the views expressed by Dr. Highman.

DR. PAUL E. BECHET: I believe that the eruption is a dermatitis medicamentosa due to the injections of a gold compound. The fact that the eruption started after the treatment had begun is also corroborative.

DR. HOWARD FOX: I agree with previous speakers that the eruption is due to a gold compound and is not the diffuse type of lupus erythematosus. Dr. Highman's suggestion that a dermatitis due to gold preparations would not present numerous small, discrete patches does not accord with my experience. This is evident in a photograph of one of my cases.

DR. R. H. RULISON: I was much puzzled by the case. The patient does not complain of itching, but he seems to be a rather insensitive person. Two or three biopsies have been made to see whether gold could be discovered in the tissue, but none has been reported. My conclusion that the condition is not disseminated lupus is based on the fact that the original lesions are somewhat better than formerly. I am inclined to believe that the lesions are due to the therapy rather than to the disease.

DR. H. H. WHITEHOUSE: I agree with those who think that the condition is dermatitis due to therapy with a gold preparation. The treatment seems to have been rather strenuous—50 mg. a week for fourteen weeks; perhaps that accounts for the severity and extent of the eruption.

DR. E. R. MALONEY: I agree with the diagnosis of dermatitis due to therapy with a gold compound.

DR. GEORGE M. MACKEE: Dr. Highman was right when he directed attention to the difficulty of interpreting a case of this kind. Most of the clinical features favor a diagnosis of dermatitis due to a heavy metal. The patch tests, however, are unreliable. A high dilution should be used.

DR. H. J. SCHWARTZ: There were many puzzling features in the case. When Dr. Fraser and I first saw the condition we were inclined to regard it as disseminated lupus erythematosus. Most of the members of the staff disagreed with that diagnosis. In regard to the clinical condition, Dr. Lewis, who has been observing the patient, definitely claims that the original discoid lupus erythematosus shows improvement. The patient has no constitutional disturbances associated with the generalized eruption. The presence or absence of gold in the tissues would be of no etiologic significance. In view of the number of injections the patient has had, gold might well be present without necessarily being the cause of the eruption.

Further patch tests with higher dilutions of gold sodium thiosulphate will be performed in an attempt to establish whether or not sensitization to gold is present.

MONILIA INFECTION OF THE MOUTH. Presented by DR. EUGENE F. TRAUB.

A boy, aged 11 years, born in the United States, has had an eruption in the mouth for eight years, that is, since about 3 years of age. In spite of active treatment during this period, only temporary relief has resulted. The lesions are found at the angles of the mouth, on the buccal mucosa on both sides and, in fewer numbers, along the margin of the gums; they are particularly numerous on the palate and on the dorsal and lateral surfaces of the tongue. Along the edges of the tongue the eruption seems almost warty, but elsewhere there are slight erosion and loss of tissue, the surface of the mucous membranes having a milk-white appearance. The patient gives a history of having had injections of arsphenamine, innumerable mouth washes and fulguration of the lesions, with little change in the condition. He has also been given an alkaline mouth wash which apparently caused slight improvement, but the condition fluctuates so from day to day that it is difficult to determine how much permanent change has been affected. Monilia were grown from all sites. The Wassermann test was negative.

DISCUSSION

DR. W. J. HIGHMAN: How can it be proved that Monilia is the agent in the case?

DR. FRED WISE: I think that a patient who has had trouble like this since infancy should be subjected to careful examination, especially with reference to the gastro-intestinal tract.

DR. GEORGE M. MACKEE: I have seen a number of patients with stomatitis, apparently caused by Monilia, who were cured with applications of tincture of iodine.

DR. EUGENE F. TRAUB: The diagnosis of moniliasis is beyond question in this case, but whether Monilia is a secondary factor superimposed on some other condition is debatable. Unfortunately, as presented, the eruption is much improved following the use of a mouth wash. It may be observed that the boy apparently has a scrotal type of tongue, and this may account for some of the persistence of the eruption at that site. This would, of course, offer no explanation for the other lesions, which have been almost equally persistent. An examination of the stools was to be made before this meeting, but through an oversight it will not be made until later. I have read several case reports in the literature, and the description of the eruption in these patients closely tallies with the appearance seen in the present case. The cultures were positive for Monilia in all the areas.

DR. GEORGE M. MACKEE: The presence of fungi in a case like this is presumptive evidence. Finnerud found Monilia in a large percentage of cases of perlèche, and fungi are often found in cases of stomatitis.

DERMATITIS ARTEFACTA. Presented by DR. GEORGE M. MACKEE.

This patient was presented before the society in December 1932, and again in January, 1933. The lesion was on hte thumb. It was not until March 15 that the patient was hospitalized and a plaster of paris cast was placed on the thumb. The lesion disappeared completely in less than two weeks. The cast was removed when the patient was presented, and the thumb was found to be normal.

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. EUGENE F. TRAUB for DR. C. M. WILLIAMS.

A girl, aged 11 years, presents lesions of one and one-half years' duration. Over the sternum is a firm, irregular elevation resembling keloid, but scattered over the rest of the trunk are firm masses, in the skin, covered with apparently normal epidermis, some of which have a slightly yellowish tingue. These feel hardly firm enough for keloid or for fibroid tissue, and a diagnosis of xanthoma tuberosum multiplex is suggested.

DISCUSSION

DR. W. J. HIGHMAN: I saw the patient this month or the month before at the departmental conference of Mount Sinai Hospital. As far as I can recall, the only lesion then present was the outstanding one on the chest. Most of the members thought that this was keloid. I do not know what the newer lesions are. They do not look like early keloids. They belong to one of the various toxic exanthems. I do not know on what the presenter's opinion was based, or why he thought that the condition was a tuberous xanthoma.

DR. FRED WISE: The absence of a yellow color makes the diagnosis as presented seem doubtful. From the clinical standpoint, the condition may be fibromatous—cutaneous fibrous nodules—rather than keloidal growths.

DR. HOWARD FOX: I do not think that any diagnosis except fibroma or keloid would be reasonable.

DR. R. H. RULISON: I agree with the previous speakers.

DR. F. C. COMBES: I also agree with the previous speakers, but I do not understand about the time element. It seems to me that the duration of the lesions is far too brief for the development of fibrous tumors like these.

DR. PAUL E. BECHET: The lesion on the chest is probably keloidal; I do not think it has anything to do with the lesions on the back. I agree with those who are opposed to the diagnosis of xanthoma, but I cannot suggest a diagnosis.

DR. GEORGE M. MACKEE: Dr. Williams must have had a good reason for suggesting xanthoma. The lesion does not look like xanthoma. I cannot make a diagnosis. I agree that the lesions suggest fibroma or keloid, but the rapid evolution and the numerous lesions may mean fibrosarcoma or some other variety of sarcoma.

DR. H. J. SCHWARTZ: I agree with the clinical diagnosis of fibroma.

DR. F. J. FRASER: Dr. Williams must have had some good reason for his diagnosis. On clinical grounds alone, I should hesitate to make a diagnosis of xanthoma.

DR. H. H. WHITEHOUSE: Dr. Williams may have tested the lesion with the diascope and found the yellow color. I see no evidence of xanthoma, however, in the clinical picture as presented.

DR. EUEGNE F. TRAUB: I am sorry that I did not have more information to present with the patient, but only the slip with the brief history was turned over to me this afternoon. I am sure that Dr. Williams will attempt to get more information about the biopsy specimen taken at Mount Sinai Hospital. Recently I reported nine cases of dermatofibroma (noduli cutanei), in none of which did the lesions clinically resemble those presented in this case. In Dr. Williams' case, the lesions are all elevated and comparatively soft, and clinically, they suggest, to me, an inflammatory process. In my cases of dermatofibroma, on the other hand, the lesions were rarely, if ever, elevated above the surface of the skin; they were hard and solid and extended deep into the tissue; the older lesions showed some central depression, and the entire process showed a downward growth rather than a rounded, elevated surface.

Book Reviews

Light Therapy. By Frank Hammond Krusen. Price, $3.50. Pp. 186, with 33 illustrations. New York: Paul B. Hoeber, Inc., 1933.

This is a useful, practical and timely volume. It discusses clearly the various types of light and their advantages and disadvantages, indications and contraindications in therapy. There are useful comments on various lamps which are on the market. In the chapter devoted to diseases of the skin, which, as it should be, is one of the most important in the book, the consideration is conservative, and the recommendations are intelligent. This chapter follows closely the recommendations of the Council on Physical Therapy of the American Medical Association. There are numerous quotations from the literature, which has been reviewed, condensed and classified so that the book is a valuable source of information.

Books Received

Beitrag zur Pathologie und Epidemiologie der Pellagra. By Priv. Doz. Dr. E. G. Nauck. Price, 3.60 marks. Pp. 44. Leipzig: Johann Ambrosius Barth, 1933.

Eine statistische Untersuchung über Syphilis. By H. J. Källmark. Paper. Pp. 229. Uppsala: Appelberg, 1931.

Studien über das Ulcus rodens. By C. Thesleff. Pp. 158. Jena: Gustav Fischer, 1933.

Der dialektische Materialismus und die klinische Medizin. By Prof. J. Lifschitz. Paper. Pp. 80. Kharkov: Medwydaw, 1932.

Handbuch der Haut- und Geschlechtskrankheiten. Volume XXIII. Edited by Josef Jadassohn. Price, 88 marks. Pp. 642. Berlin: Julius Springer.

Melioidosis. By A. T. Stanton and William Fletcher. Pp. 94. London: John Bale Sons & Danielsson, Ltd., 1932.

Cutaneous Neoplasms. By C. Norman Paul. Price, 10 shillings, 6 pence. Pp. 150. London: H. K. Lewis & Co., Ltd., 1933.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Alberic Marin, President, Drummond Medical Bldg., Montreal.
Antonio Sabetta, Secretary-Treasurer, 3435 St. Denis St., Montreal.
Place: Hamilton, Ontario. Time: 1934.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. Guy Lane, Chairman, 416 Marlboro St., Boston.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Cleveland. Time: June 11-15, 1934.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.
Place: Pittsburgh. Time: 1933.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.
Place: Iowa City. Time: October 10, 1933.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.
Place: Boston. Time: April 11, 1934.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November 14-17, 1933.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.
Place: Jacksonville. Time: July 2, 1934.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania Section on Dermatology

Stanley Crawford, President, 200, 9th St., Pittsburgh.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

G. H. Belote, Chairman, 201 S. Main St., Ann Arbor.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.

Minnesota Dermatological Society

E. Z. Shapiro, President, 14 W. Superior St., Duluth.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

Everett C. Fox, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Houston. Time: Fall, 1933.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Samuel Feldman, Chairman, 1955 Grand Concourse, New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Louis J. Frank, President, 1367 Eastern Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo Dermatological Society

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Max Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

S. Littman, President, 10515 Carnegie Ave., Cleveland.
H. G. Miskjian, Secretary, 856 Rose Bldg., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Howard Fox, Chairman, 140 E. 54th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, 1538 Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

New York Dermatological Society

Edward R. Maloney, President, 853 7th Ave., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

Alfred Schalek, Chairman, 721 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Jacques P. Guequierre, Chairman, 1930 Chestnut St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Frederick Amshel, Chairman, 3401 5th Ave., Pittsburgh.
Bernhard Goldmann, Secretary, Jenkin's Arcade, Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Ernest K. Stratton, President, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.